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# The American Journal of Syphilis

A QUARTERLY JOURNAL DEVOTED TO THE  
STUDY AND PREVENTION OF SYPHILIS

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## Original Articles

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### THE INTRAVENTRICULAR TREATMENT OF PARESIS

BY NORMAN SHARPE, M.D., NEW YORK CITY

(Received for publication, December 14, 1917)

THE subject of paresis has been keenly revived in the last few years. The discovery of the spirochete pallida in the cerebral cortex by Moore and Noguchi was quickly followed by the Swift and Ellis procedure of intraspinal injections of salvarsanized serum. Then came the Ogilvie modification of this method, by adding definite quantities of salvarsan to the already salvarsanized serum, and injected intraspinally; and later the injection of salvarsan solutions under the cranial dura as done by Marinesco and practiced and reported in this country by Wardner, Cotton, and others. Their reports show that by these methods they have obtained distinct and marked improvement both clinically and in the serology in a large proportion of the paretics treated, and in some early cases an apparent definite arrest. However, in the treatment of paresis, both the intraspinal and subdural methods labor under disadvantages. As demonstrated by the animal experiments of Goldmann, Weed, Tilney and Woolsey, solutions introduced intraspinally have difficulty in diffusing; the larger part is drained off in the venous channels

at the base of the brain, and only a small part succeeds in reaching the cerebral cortex where it is essential to have it. The disadvantage of the subdural method is that solutions injected subdurally are still without the arachnoid, which must be penetrated to reach the cortex. Under normal conditions a solution will easily do this, but in paretics the arachnoid is thickened, whitish and opaque, through which it is evident that a solution will have difficulty in diffusing.

Impressed by the results of these investigations, the writer carried out a series of experiments on animals, injecting staining solutions into the lateral ventricles. As they have been described in detail elsewhere,\* only the results will be discussed here. It was found that staining solutions injected into the lateral ventricles of dogs, spread over the entire cortex both of brain and cord, including the ventricular system, extending to the depths of all the sulci, and forward to the olfactory bulbs and the retrobulbar spaces of the eye. In the dogs injected subdurally, the staining was confined to the hemisphere of that side, and did not extend to the depth of the sulci, nor enter the ventricular system. The results of injecting staining solutions intraspinaly, as mentioned above, show that very little succeeds in reaching the cerebral cortex. As these experiments demonstrated conclusively that solutions introduced into the lateral ventricle excelled in the extent and facility of diffusion, it was evident that salvarsan solutions by this procedure could reach the spirochete more effectively, and Dr. Hammond and I determined to employ this method in the treatment of paresis. The first injection was given in January, 1915. Since that time we have treated by the intraventricular method a number of cases, of which number the first thirteen were treated at dates sufficiently remote to allow us to draw some conclusions as to the value of this method. These 13 cases were those treated in the period of two years between January, 1915, and December, 1916. In the first few cases 0.6 mg. of salvarsan was given in blood serum; in one or two instances 0.6 mg. salvarsan in salvarsanized serum. Three intraventricular injections were given each patient at intervals of three weeks. Beyond an occasional headache and slight rise in temperature there were no unfavorable reactions, and the patients usually left the hospital

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\**Jour. Am. Med. Assn.*, Dec. 18, 1915, lxxv, 2147.



on the fourth day. Following the three injections, we advised a rest period of several weeks and then a return to the hospital for fluid examination, and if indicated further intraventricular treatment. As the reactions (headache, fever) following the injections were so slight, we gradually raised the dosage in succeeding cases until at present we give 1 mg. salvarsan in salvarsanized serum as the initial dose, and 1.8 mg. in the third injection. The reactions (fever, headache) following the latter quantity have been no more severe or frequent than those seen after the smaller dosage. This quantity (1.8 mg.) is about double the amount that can be safely given intraspinally.

The plan of introducing a rest period following the three injections, though we considered it good treatment, did not work out very well in the case of some of the clinic or free patients. If during the rest period the patient showed but little or no improvement, the relatives became discouraged; on the other hand, if marked improvement occurred, especially if the patient was able to return to work, even though the later fluid reactions were positive, further treatment was apt to be refused on the ground that it was unnecessary. This led to the undoing of two of our most promising cases. One of these had not been able to work for fifteen months before treatment. Marked improvement followed injection, and three months later he returned to work. Though fluid reactions were still positive, he refused further treatment, and a relapse occurred one year later. In the other patient his long freedom from parietic symptoms following three injections makes his case interesting, and it is presented in more detail, as follows:

J. M.—Lues fifteen years ago. In the latter part of 1914 he began to complain of headache, was easily fatigued, could not do his work properly. His relatives noticed nervousness, irritability, changed disposition, attacks of weeping, depression, queer utterances. Was forced to quit work at this time. Came to us March, 1915. Examination showed unequal pupils which did not react to light, tremors of lips and occasionally of face, exaggerated knee-jerks, slight dysarthria, inability to "carry" figures or answer questions intelligently. Blood Wassermann was positive, spinal fluid Wassermann positive, globulin increased, cells 10, colloidal gold test gave the parietic curve. He was given three intraventricular injections.

tions of salvarsan in blood serum. During the rest period he improved so much that further treatment was refused, though the fluid reactions were still strongly positive; and he returned to his former work in the fall of 1915, and worked steadily for two years. Examination during this time by different neurologists found him, except for the Argyll-Robertson pupil, free from the clinical symptoms of paresis though the fluid reactions were still positive. Two months ago he had a sudden relapse and was removed to a hospital. The outlook for this case under thorough and persistent treatment would have been most promising.

The criticism was made in a recent article\* that those practicing intradural treatment of syphilis centered their interest chiefly on the changes in the serology, and have been prone to mistake the changes and reductions in cerebrospinal fluid laboratory findings as proof of clinical improvement of the patient. The contrary has been our experience. In the great majority of our cases, the clinical improvement preceded the fluid changes, and in several cases in which most marked improvement occurred clinically, we succeeded in influencing the fluid reactions but slightly.

In the thirteen cases of this series receiving intraventricular treatment there were no deaths and no accidents attending injection. Though in many of them there was a twenty-four-hour rise in temperature accompanied by headache, yet at no time were the reactions severe enough to give rise to any anxiety. Two of the thirteen cases, rather advanced ones, showed no improvements from the injections and died several months after the final injection in the terminal stage of paresis. Two others, one of whom received only one injection, were not improved, and were later committed to asylums. The remaining nine showed decided improvement, chiefly in the clinical symptoms. They were less emotional, their memories were better, they were improved mentally and physically, and some of them are still improving. Five of the nine showed marked improvement. These five, following the rest period after three injections, were able to return to work, and have been working for from ten months to two years. In only two of these five did we succeed in rendering the fluid findings negative; in one this occurred after he received a second series of injections one year after the first. This

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\*Sachs, B.: Jour. Am. Med. Assn., Sept. 1, 1917, Ixix, No. 9, 681.

was done solely on the fluid findings, as there had been no relapse in the clinical improvement. He has been at work for eighteen months. Two of the five cases refused further treatment, though the later fluid findings were positive, and they have lately relapsed. These two cases illustrate the disadvantage of having the rest period follow three injections only, especially in clinic cases. They are apt to drift away, and if marked improvement occurs, to refuse further treatment. It will undoubtedly be better judgment to continue the initial series of injections, given at two or three week intervals, ignoring the clinical improvement, until the fluid is rendered entirely, or almost entirely, negative, or until the point of tolerance is reached, before the rest period is inaugurated. Though this will entail more careful scrutiny of the patient's general condition during treatment, it will lessen the possibility of the regrettable and probably preventable relapses mentioned above.

When I stated that we had rendered the fluid negative in some instances, I was speaking of the Wassermann reaction, the cell count and the globulin content. In no instance have we more than temporarily reduced the typical paretic curve of the colloidal gold reaction. Examination of the fluid at a later date always revealed the full paretic curve. This has also been the experience of other observers. Whether the gold reaction, which is the most constant and reliable laboratory finding in paresis, and which persists after the Wassermann has disappeared and the globulin been reduced to normal, is indicative of the continued presence of the spirochete and, therefore, points to further treatment, or whether once established it is unchangeable even if the disease process is eradicated, will be determined only by future experience. The gold reaction is found very early in the disease, and is of immense help in diagnosing those early cases of paresis where the clinical symptoms are few and slight. In fact our experience with it in two cases was such as to give rise to the suspicion that it may even antedate the clinical symptoms. One of the 13 cases, who came to us in the latter part of 1915, had been given by others a large number of intraspinal injections for early tabes. The lightning pains, ataxia and bladder symptoms had disappeared and the only remaining clinical signs were the absent lower tendon reflexes and the Argyll-Robertson pupil. He came to us complaining of headache, and learn-

ing of his tabetic history, we examined the spinal fluid. It was negative except for the gold reaction which gave a typical paretic curve. There were no clinical symptoms of paresis present, except perhaps a faint tremor of lips and tongue. After several weeks he developed mild slurring of speech, easily seen tremor of tongue and lips, mental depression, occasional attacks of weeping and mild delusions. He was given five intraventricular injections in ascending doses. During the rest period of several months the above symptoms disappeared and he was able to return to work. A year later the paretic curve of the gold reaction was still present. He has been at work now for eighteen months. The other case, not in this series, was also a tabetic in whom paresis was not suspected. Repeated examinations of the fluid over a period of three months gave the typical paretic curve in every test. During the latter part of this period faint tremor of lips appeared, and intraventricular treatment was decided upon. Three injections were given, the dosage ascending from 1 mg. to 1.8 mg. He is still under observation. No evidences of deterioration are present. If further experience shows that the colloidal gold paretic reaction is constant in the very earliest stage of the disease process, or better still, that it antedates the recognizable clinical symptoms, we shall have a most valuable aid in combating paresis at the time when treatment promises most.

Only two cases of this series of 13 could be termed early cases. The observed symptoms had existed for from 6 to 20 months; in several of them, however, the deterioration was but slight and it is in these cases that we have obtained the maximum improvement.

The relatively small amount of salvarsan that is used in any method of intradural treatment has been adversely commented upon, as compared with the intravenous dose. But when we consider the great disparity in volume of the two circulating media (the blood and cerebrospinal fluid), we find that the quantity given intraventricularly is relatively not minute. The solution used in ventricular injection consists of 12 c.c. blood serum and 13 c.c. saline solution. To equal the quantity of salvarsan per cubic centimeter of blood when the full intravenous dose of 0.6 gm. is used, would require in the ventricular serum 3.5 mg. of salvarsan. This is less than double the quantity we have given, for the 1.8 mg. of salvarsan is added to already salvarsanized serum.

The day preceding injection, the patient is given a full intravenous dose of salvarsan or arsenobenzol and within the next hour 40 to 60 c.c. of blood is drawn off into a sterile needle and tube. The various steps in the preparation of the serum are carried out the following morning.\* The operative technic is reasonably simple and has proved entirely safe. Under ether anesthesia a small skin flap or straight incision is made a little in front of bregma and 2.5 cm. to the right of the median line, overlying the first frontal convolution. A small button of bone is removed by the trephine and a small dural incision of one-eighth inch is made. A slender cannula having a blunt point and openings on the side is introduced at a point free of cortical vessels, and passed downward and a little backward into the lateral ventricle. The head of the table is lowered and 20 to 30 c.c. of fluid allowed to escape. The head of the table is then raised and a funnel containing the serum is attached to the cannula by short rubber tubing. The serum is slowly introduced and enters entirely by gravity. The cannula is then withdrawn and scalp wound sutured. It is not necessary to suture the small opening in the dura, as it is plugged by the arachnoid, preventing the escape of fluid. The whole procedure requires from 20 to 35 minutes, the greater part of which time is consumed in the withdrawal of the fluid and the introduction of the serum. The patient is allowed to sit up in 24 hours, and leaves the hospital in from 3 to 4 days. In second and subsequent injections the scalp over the trephine opening is infiltrated with novocaine and the ventricular injection carried out as described above. The brain not being sensitive, a general anesthetic is not necessary in second injections. A sharp-pointed needle or cannula should never be used to puncture the ventricle, nor should force be employed in the introduction of the serum. Disregard of this will sooner or later be followed by serious hemorrhage and other complications.

As no unfavorable reactions have followed our present maximum dose of 1.8 mg., we intend to gradually increase the quantity in subsequent injections, though we believe 1 mg. to be the safest maximum initial dose. It is reasonably certain that in the not distant future other preparations possessing the spirocheticidal power of

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\**Jour. Am. Med. Assn.*, July 7, 1917, lxi, 23-27.

salvarsan, with less toxicity, will be devised, facilitating greatly the treatment of paresis and allied conditions.

Prompt examination of the spinal fluid should be made in all patients showing the slightest signs of involvement of the nervous system. This is especially true of those cases presenting symptoms of easy fatigue and depression, usually ascribed to overwork or neurasthenia. It will reveal many cases of early paresis in the stage when treatment will avail most.

The improvement following injection has been assumed by some to be the natural remission occasionally occurring in untreated paresis. When we know that asylum statistics unite in declaring 6 per cent to be the maximum of natural remissions, the discrepancy between this and the 20 to 50 per cent (of different reports) of remission following intradural treatment, is too wide to be bridged by such an assumption.

We believe that it has been conclusively demonstrated that intradural injections of salvarsan are of marked benefit in the treatment of paresis, and we believe that the spirochete can be most effectively attacked through the ventricular route. We have not found that ventricular injection has any effect in even retarding advanced cases, and advise its use only in early cases, where deterioration is not marked. In these cases it holds out the best hope of benefit that we know of today.

## SYPHILIS OF THE INNER EAR AND EIGHTH NERVE

By GEORGE W. MACKENZIE, M.D., PHILADELPHIA, PA.

(Received for publication, December 19, 1917)

**B**ECAUSE of its prevalency, existing much oftener than is generally supposed; because of its rapidity, resulting in irreparable damage to hearing in a relatively short space of time where treatment has been neglected; because of its amenability to well established forms of treatment when instituted early; because of its character permitting of a ready diagnosis by a few clinical tests and equally certain laboratory findings; syphilis of the inner ear and eighth nerve is a subject that commends itself to the earnest consideration of the syphilologist no less than to the otologist.

The otologist in recognizing the clinical picture of syphilis of the inner ear and eighth nerve bears the same relationship to the internist as does the ophthalmologist who recognizes the characteristic retinal changes of nephritis. It would be difficult to say which of these two specialists has the more important message to convey to the internist.

Concerning its prevalency, Fraser<sup>1</sup> claims "there is reason also to believe that many cases of congenital deafmutism are really due to intrauterine syphilis or to syphilitic changes in the ear occurring before the child has learned to talk. Statistics as to the frequency of deafness in children suffering from congenital syphilis vary very greatly. Some authorities—Carpenter puts it as high as 60 per cent. others only at 33 per cent."

According to the same authority, it has been recently found that one-third of the cases of nerve deafness of unexplained origin have a plus Wassermann reaction, thus pointing to a probable syphilitic origin.

According to the findings of Drs. Browning and Cruickshank<sup>2</sup> who conducted the Wassermann reaction in the series of cases studied by J. K. Love:<sup>3</sup> "When considering the etiology of sporadic congenital deafness in the light of the Wassermann reaction, it is necessary to bear in mind exactly what information this test affords. A positive

reaction is the rule when there are signs of active disease due to a wide dissemination of the causative agents throughout the body; on the other hand, when the disease has become latent, or where the activity of the parasites is limited to a small area, the reaction is negative in fully 50 per cent of cases. Thus a negative reaction can not be taken as a complete proof that syphilis is absent; it may equally well occur when a once active infection has become dormant."

This has been my experience as well as that of many others. In those cases where the clinical diagnosis was quite certain while the laboratory diagnosis was negative, the therapeutic test with mercury and especially potassium iodide has rather borne out the clinical diagnosis. I can not say invariably so, for the reason that it must be conceded that these remedies act beneficially in other pathologic conditions besides syphilis. When we include in the list the cases of deafness from meningitis of childhood, presumably due to the meningococcus of Weichselbaum, but in fact due to the syphilitic poison, it will be found that syphilis in one form or another is a far greater cause of deafness than is generally credited.

According to Busch,<sup>4</sup> quoted by E. Vály,<sup>5</sup> in 52 per cent of acoustic (eighth nerve) lesions the Wassermann was positive. It does not state whether this includes both the unilateral and the bilateral cases. Furthermore, these figures would not include those cases due to syphilis, where for well-known reasons the Wassermann can be negative in spite of the presence of syphilis, as pointed out by Brown-ing and Cruickshank and many others. Vály mentions the well-known fact that the great number of acoustic nerve paralysis in lues proves that the eighth nerve is less resistant to the specific poison of syphilis than the other cranial nerves.

According to Gerber,<sup>6</sup> luetic eighth nerve affection is as a rule bilateral. When it appears unilaterally, it occurs as a result of a far advanced affection of the blood vessels.

In the absence of a history pointing to a basal skull fracture or meningitis, primary bilateral internal ear or nerve deafness occurring in an adult, is according to G. Alexander,<sup>7</sup> due, four times out of five, to acquired syphilis. I would add that in the remaining one-fifth it is due to congenital syphilis. Bilateral nerve deafness may in very exceptional instances be due to other causes, but they are so



few as to be almost negligible. In the case of primary unilateral internal ear or nerve deafness, the contrary holds true, syphilis being a rather exceptional cause.

Concerning its rapidity, the course of labyrinthine syphilis is rapid, according to the observations of von Troeltsch, Roosa, Hutchinson, Schwartz, Knapp, Buck, Baratoux, and Hermet, quoted by Politzer.<sup>8</sup> The same author mentions a case that he saw where deafness was almost complete seven days after the impairment of hearing first began. Cases occur, however, in which the impairment is more gradual, remaining stationary for a long time (months or even years), followed by an abrupt and complete loss.

Alexander,<sup>9</sup> in referring to labyrinthine syphilis, claims that the degeneration of the neuroepithelium and nerve fibers is rapid.

The impairment of hearing begins suddenly, attacks both sides and is pronounced from the beginning and progresses uninterruptedly to complete deafness (Bezold).<sup>10</sup> In the case of acquired lues in the opinion of Vályi, impairment of hearing begins suddenly and progresses rapidly. In the congenital form, on the contrary, deafness begins more gradually, from the 6th to the 10th year of life. Occasionally, in children the course may be so rapid that the child may become completely deaf over night. (Urbanschitsch)—the so-called *typus apoplectiformis*.

In speaking of inner ear syphilis, Stein<sup>11</sup> claims that the deafness is rapid in its progress and soon becomes quite profound. There is no preponderance of lost hearing in either the upper or lower end, but the entire scale, as a rule, is affected with occasional islands of hearing for a little while. He refers to nerve deafness as coming on quite suddenly; in fact, often overnight or after some prolonged exposure or exertion. Occasionally it may appear rather suddenly and progress with only fair rapidity.

In the acquired form the earlier the symptoms of labyrinthine syphilis manifest themselves, the more sudden is the onset, and the more rapid its course and vice versa.

In view of the relative dearth of carefully studied material, both clinically during life and subsequently by patho-anatomic methods, and because of the wide variation in the character of the lesions thus far found in the inner ear and nerve, it becomes a difficult, if not a quite impossible task for one to offer fast and hard

rules as to the relative rapidity with which the functions (hearing or equilibrium, or both combined) may be lost in any particular form of syphilitic lesion. Suffice it to say, that in the vast majority of cases the loss of functions is quite rapid. In other words, given a case of bilateral deafness, beginning suddenly and advancing rapidly, there is the strongest probability, in the absence of a definite history to the contrary (skull fracture, meningitis or recent acute severe fever), that the deafness is due to a syphilitic lesion in the inner ear and eighth nerve.

Concerning its amenability to treatment, an active syphilitic lesion of the inner ear or eighth nerve is just as responsive to anti-luetic treatment (salvarsan, mercury or potassium iodide) properly selected and early begun as the same type of lesion located in any other part of the body. I have amply proved this in a fairly wide experience.

On the other hand, those cases which present themselves late, after the functions have already been destroyed, the prognosis is quite unfavorable in spite of treatment. Furthermore, salvarsan, mercury, and potassium iodide, do not possess the same curative properties in all stages of the syphilitic process. For instance, potassium iodide administered alone in a recent active syphilitic lesion, where the spirochetes are active, is of very little value compared with salvarsan or mercury. In a late case, let us say of gray atrophy of the nerve following a syphilitic basilar meningitis years before, and where the spirochetes may be absent, potassium iodide is of far greater value than salvarsan or mercury. In the selection of the remedy to be used there must be some understanding of the condition present; i. e., a correct diagnosis so far as it is possible to make one by clinical and laboratory methods; besides, it is essential to know just what action these remedies will have upon the various types of syphilitic and postsyphilitic tissue change.

Recently, and especially in the Vienna clinics, the question has been raised as to the advisability of using salvarsan indiscriminately in all cases of early syphilis, for fear of the danger of exciting pathologic changes in the optic and acoustic nerves from the arsenic contained in the salvarsan.

During the last four or five years, a great deal has been written on the subject, both pro and con. The present attitude of the

otologic profession is that most of the suspected cases of arsenic toxemia are really cases of neurorecurrences of syphilis.

Benario<sup>12</sup> (quoting from Duel<sup>13</sup>) who had collected the largest number, had reported 14,000 cases in which there had been neurorecurrences in 126. Out of these, 118 occurred in the primary or secondary stage. The recurrences took place in the second to the eighth nerves in the following proportion: auditory 43 per cent, optic 26 per cent, facial 15 per cent, the balance divided among the other four. Neurorecurrences occurred in 96 per cent of the cases within four months after the administration of the salvarsan, 40 per cent occurring in the second month. The explanation which they gave was that the dose of salvarsan had been insufficient to completely destroy all of the spirochetes. In support of this contention they advance the following reasons.

"First, the length of time intervening between the administration of the salvarsan and the neurorecurrences.

"Second, the irritative and inflammatory character of the nervous phenomena, as compared with the atrophic changes observed after the administration of other arsenic preparations like arsacetin.

"Third, the appearance of the affection in the early stages of syphilis.

"Fourth, when salvarsan has been given in other affections, the neurorecurrences have not appeared.

"Fifth, the manifestations have improved or disappeared under mercurial treatment or another administration of salvarsan.

"Sixth, the neurorecurrences have almost invariably appeared in cases where small or inadequate doses of salvarsan have been given.

"Seventh, similar manifestations have appeared while mercury was being given."

Joseph Beck<sup>14</sup> reported forty-seven cases of syphilis of the nose and throat treated with salvarsan, most of them in conjunction with mercury and potassium iodide. All of the cases presented a strongly positive Wassermann reaction. In not a single instance was there any trouble with the ears following the injection, except a ringing, which disappeared within a day or two. Near the close of his article, Beck states that since this article was read, the author has treated about twice as many cases of this kind and has observed no untoward effects from the use of salvarsan.

Concerning neurorecurrences, the opinion expressed by Beck has been shared by numerous writers, both before and since his publication, and it is the prevailing opinion today. This opinion is shared in by Ehrlich,<sup>15</sup> Urbanschitsch,<sup>17</sup> Benario,<sup>18</sup> Werther,<sup>19</sup> Knick,<sup>20</sup> Willcutt,<sup>21</sup> and a host of others.

Ehrlich<sup>16</sup> recognizes in the acute eighth nerve manifestations that follow the administration of salvarsan, one of the manifestations of the Jarish-Herxheimer reaction, for the tinnitus and vertigo appear almost simultaneously with the skin reaction and both disappear together. He believes that there is an analogous swelling in the region of the nerve as in the skin, and the resulting pressure on the nerve is responsible for the nerve symptom.

Concerning its character, authorities generally agree that the clinical picture of syphilis of the inner ear and eighth nerve is sufficiently characteristic to permit of a ready diagnosis.

Independent of the history as to whether the patient had suffered a primary lesion or not, which is often unreliable, there is sufficient in the history referable to the ears alone to afford us a valuable hint. In the majority of cases of acquired syphilis the history is that of pronounced impairment of the hearing function that came on suddenly; often they will tell us that the impairment came on after an unusual strain or weather exposure. In the history they will often complain of a single ear being affected, but upon functional examination the other will be found more or less affected after the same manner as the one complained of. In other cases the patients tell us that both ears are affected, but one more than the other.

The functional tests will show a diminution of hearing to the conversational and whispered voice, to the acoumeter and the watch, to the high, low, and middle tone forks. It has not been my experience to find the perception to the high tones diminished out of proportion to the low, as was formerly claimed. Some cases will show a greater diminution for the high than for the low tones, while others will show the opposite condition. Examination of the whole gamut will frequently show relative scotoma, even where the hearing for the remaining tones is comparatively good. In still other cases there is a marked contraction at both ends of the scale, while for the medium tones there is comparatively good hearing.

The Weber, Schwabach and Rinne tests are quite characteristic,

in that the Weber is lateralized to the poorer hearing ear, the Schwabach (bone conduction) is shortened and the Rinne (bone conduction compared to air conduction) is positive; that is, bone conduction is diminished in about the same proportion as air conduction, allowing of a shorter bone than air conduction.

Wanner,<sup>22</sup> Beck,<sup>23</sup> Willcutt<sup>21</sup> claim that even in cases of syphilis without apparent reduction in air conduction, the bone conduction is relatively short, and they dwell upon this finding as a characteristic sign of syphilis.

In addition to these characteristic findings of syphilis of the inner ear involving the cochlea, there may or may not occur symptoms occasioned by involvement of the vestibule and semicircular canals when the syphilitic process involves these parts. The symptoms referred to are vertigo and equilibrium disturbances with nystagmus to one or the other side depending upon the character of the lesion and which side is the more involved. But before taking up the details of diagnosis, which is one of the most interesting of otologic subjects, it occurs to me that it would be more in order to first discuss the subject of the pathology, for, as we shall see, the pathology varies considerably in different cases according to the location of the lesion, whether the inner ear or nerve is involved or both together; whether the process is a primary or secondary one; whether the existing pathologic condition is caused directly by the presence of a syphilitic exudate or infiltrate, or indirectly due to the presence of a nearby syphilitic process; whether the condition is the result of an acute active syphilitic infection or happens to be the aftermath of some previous meningeal or cranial bone involvement.

Fortunately for us, no matter what the form of syphilitic involvement is or where the lesion is located (the inner ear or nerve), the history and findings are so characteristic and vary so slightly, that the diagnosis ordinarily is quite an easy matter. Furthermore, there are sufficient variations combined with differences in the test findings as to permit us to make a still finer diagnosis localizing the lesion, and at least its clinical character (irritative or destructive).

If we are to accept the findings of all authorities with equal value, then we must accept:

That syphilis may affect the inner ear alone, the eighth nerve alone, or both combined.

That syphilis may involve the inner ear primarily or consecutively to syphilitic processes originating in the middle ear or the eighth nerve. Syphilis of the nerve may involve a single branch, cochlear or vestibular, or both combined.

That syphilis may involve the nerve directly by a syphilitic process originating in the nerve (neuritis) or indirectly by pressure due to narrowing of the bony canal, adjacent intracranial gumma, or low grade basalar meningitis.

That syphilis may affect the eighth nerve of one side (very rarely) or both sides (very commonly).

That syphilis of the eighth nerve may occur as a mononeuritis or a phenomena of a polyneuritis where the II, V and VII nerves more commonly take part in the process.

That syphilitic involvement of the inner ear and eighth nerve may occur incidentally in the case of gummatous infiltration of the cranial bones, especially the temporal.

That syphilis may attack the inner ear and eighth nerve during the secondary, tertiary or very late metaluetic stage. We are justified in referring to the very late manifestation of lues (tabes and dementia paralytica) as a distinct stage of syphilis even in those cases where the Wassermann is found to be negative.

That syphilitic inner ear involvement, coincident with the secondary skin and throat manifestations, may have been observed as early as the seventh day after the primary infection by no less an authority than Politzer.

The poison of syphilis manifests itself in the presence of a middle ear suppuration actively due to any of the acute infectious diseases in such a manner as to favor the extension of the suppurative process to the inner ear. In other words, in a series of cases of acute middle ear suppuration, there will be a far greater proportion of inner ear complications among the syphilitics than among the non-syphilitics; besides, a mild catarrhal inflammation of the middle ear that would ordinarily respond promptly to mild treatment in a non-syphilitic may act as a sufficient irritant to excite an active syphilitic lesion in the inner ear of one suffering from general syphilis, just as noxious influences of any kind including mechanical injury tends to precipitate a syphilitic lesion at the site of the injury in one so predisposed.

Of all the cranial nerves, none is so vulnerable to the syphilitic infection as the eighth. For this reason it frequently happens that the eighth nerve is the first to feel its influence, and the otologist is thereby afforded the opportunity of being the first to recognize the general character of the disease.

Gruenberg,<sup>24</sup> in the course of his examination of the temporal bone of a seven to eight month luetic fetus, found the parasites distributed throughout the temporal bone, but especially noticeable along the vessels and nerves in the perivascular tissue in the vessel walls and only sparsely within the vessel. In the nerve the parasites were found between the nerve fibers, forming parallel layers. In the cross section of the nerves they were recognizable as distinct black points (stained by Levaditi's method). In most of the nerves they were to be found in exceedingly large numbers.

In the case of the dura of both middle and posterior fossæ the spirochetes were found in the region of the wall of the vessels as well as in the fine sensory nerve stems. They were found also in the deepest layers of the periosteal dural sheaths clear to the porous acousticus internus. Spirochetes were found in the nerve branches and in the ganglion, but were found in diminishing numbers as the nerves approached their foramina in the bone, and disappeared altogether after their entrance into the inner ear. Nowhere in the spaces of the labyrinth could spirochetes be found. In the medullary substance of the bone surrounding the labyrinth capsule, they were to be found in large numbers. They were also found in the middle ear including the marrow of the ossicles, in the facial canal and in the carotid canal, the mucous membrane of the tympanic cavity and eustachian tube, in the tensor tympani and stapedius muscles.

Their absence within the inner ear was striking. There are three possible explanations: First, the silver stain may not have reached the inner ear, in which case a second attempt would be worth while with the capsule removed in part before staining; second, the inner ear may have become fouled, as is a very common occurrence in the preparation of the inner ear for microscopic study where the capsule is left intact; third, the syphilitic infection had not yet reached the inner ear, which is the explanation I prefer.

Gruenberg's<sup>24</sup> study leads him to believe from the distribution of the spirochetes that the infection spreads by the route of the

blood vessels and nerves. Of the actual pathologic changes resulting thereby, he is in doubt, for the pathologic changes were not found proportionate to the prevalency and distribution of the spirochetes. Whether minute changes were present in the nerve or the membranous labyrinth could not be determined because of the postmortem changes.

These findings of Gruenberg rather corroborate those of Asai,<sup>25</sup> who examined the temporal bones of a series of congenital luetic fetuses and newborns in which he found no pathologic changes in the labyrinth; however, he found developmental disturbances in 25 per cent of the cases.

Concerning the striking disparity existing between the intensity of pathologic changes and the prevalency of the spirochetes, Verse concludes from his findings that the parasites are generally found in greatest numbers where there is no tissue change present, whereas they are found only sparsely where the pathologic changes are most marked, according to Hoffman.<sup>26</sup>

Panse<sup>27</sup> examined, microscopically, twelve temporal bones taken from seven cases of congenital syphilis and found, besides characteristic bone changes, hemorrhages which could not be traced to suffocation, because he had failed to find the same character of hemorrhages in other temporal bones taken from patients who had died from pneumonia, diphtheria, etc. Furthermore, in the syphilitic cases he claims to have found pigmented granules which indicate hemorrhage of longer standing than the hemorrhage which accompanies suffocation. Besides these hemorrhages, he found in one case changes in the cochlea corresponding to those which he had observed in deaf-mutism. The changes which he found in the labyrinth were hemorrhage on the crista ampullaris of the superior semicircular canal, which had furthermore grown adherent to the opposite wall. The ampulla of the inferior canal contained, in place of the normal crista, only a remnant of a crista. On the epithelium of the macula utriculi, no hairs and no otoliths were visible. In the sacculus there were no hairs present; however, the otoliths were present. The inferior end of the scala media was full of connective tissue, epithelium of the basal winding was but poorly preserved. Corti's organ was atrophic; the supporting and hair cells were indistinct. Corti's organ consisted of an indistinct heap of cells with round nuclei. The spaces



within the lamina spiralis ossea that normally contain nerve fibers, were filled instead with young connective tissue fibers. The spiral ganglion contained more round than ganglion cells. He found nowhere evidences of endarteritis obliterans or periarteritis. The acoustic fibers in the lamina cribrosa and in the stem of the nerve were richer in cells than normal.

O. Mayer<sup>28</sup> examined histologically the temporal bones of eleven cases of hereditary lues. They were from children of different ages, the youngest having lived but ten minutes, the oldest seventeen months. He excluded from his examinations the temporal bones of children who were born dead. He found in nine cases middle ear suppuration, but in none of these was there evidence of extension to the inner ear. In two cases there were hemorrhages in the middle ear. In two cases there was evidence of meningitis. In eight cases there were signs of inflammatory irritative condition of the meninges present. In only one case were conditions normal in the internal auditory canal. In the inner ear of two cases there existed a mild inflammatory condition; in four cases a slight inflammatory irritation. In the internal auditory canal Mayer found constantly the greatest changes; cellular infiltration in the acoustic nerve, especially the cochlear branch. In two cases he found hemorrhage in the nerve which he attributed to suffocation.

Mayer regards the inflammatory changes in the meninges and the eighth nerve as conditions directly due to the syphilis, while he holds the degeneration of the nerve fibers and sense epithelium in the inner ear to be the sequel of the former condition. His conclusions are, first, that in hereditary lues of children there occurs a specific inflammation of the meninges. Second, with the meningitis there occurs a specific interstitial inflammation of the acoustic (neuritis acustica hereditaria). The inflammatory process propagates or spreads toward the inner ear resulting in most cases in an inflammatory irritation (hyperaemia) only, occasionally in an exudative inflammation (labyrinthitis hereditaria).

Asai,<sup>25</sup> of Siebenmann's Clinic, examined twenty temporal bones from fourteen children ranging in age from a seven months' fetus to a two months' old child, all suffering from hereditary lues. His resume is as follows:

- (1) Of the twenty temporal bones in only one case could it be

proved that changes in the labyrinth were due to hereditary lues.

(2) The walls of the blood vessels and their surroundings (perivascular lymph space) showed no luetic changes whatever, nor could any hemorrhage be found in the organ of hearing that could be attributed to hereditary lues.

(3) Fresh effusions of blood in the inner ear are of postmortal origin. The hemorrhage in the labyrinth and middle ear present in one case depended on the suffocation.

(4) In the corpse of a three weeks' old child was found evidence of a brief lasting pachymeningitis and labyrinthitis. In this case also there were no specific changes in the vessels found, so that a causal relationship with lues hereditaria was possible but not proved.

(5) According to the findings of others, retardation, imperfection and cessation of body growth is conceded to be an important symptom of hereditary lues. Asai established by microscopic examination the counterpart of these changes in the temporal bone. He found various parts of the middle and inner ear markedly less developed than they should be for a correspondingly advanced pregnancy.

(6) In all the examined cases of hereditary lues there were found characteristic visceral and osteochondritic changes. The involvement of the hearing organ in syphilis occurred but once in intra-uterine life.

Ig. Hofer<sup>29</sup> made histologic examination of the temporal bones of ten cases of hereditary lues. Of these ten cases five were newborn, three of which lived but a few hours; two lived to be two months old. The remaining five were premature births between the seventh and eighth month of pregnancy. All ten cases showed characteristic visceral and osteochondritic evidence of syphilis. A resume of his conclusions based upon the findings are as follows:

(1) In the bone itself there occurred delayed and interrupted ossification analogous to that found in the long bones. Seven of the ten presented the appearance of delayed ossification which permitted of abnormally large marrow spaces in the bone. In only three cases was the bone developed comparable with that of the normal of corresponding age.

(2) In consequence of hereditary lues there can arise an intra-

uterine inflammatory process of the meninges of the dura and of the acoustic nerve. These changes have already been referred to and emphasized by Mayer. Two of the cases examined by Hofer showed marked evidence of a subsiding intrauterine meningitis. Under such conditions a labyrinthitis is possible, but could not be proved owing to the macerated condition of the labyrinth.

(3) Those cases in which hemorrhage occurred in the cavity of the middle ear, internal ear, and internal auditory canal are positively not dependent upon the syphilitic process, but are due solely to suffocation, as pointed out by Mayer and Asai.

It would seem, therefore, from the combined studies of Mayer, Asai, and Hofer, who studied their material most carefully, that the opinions regarding the frequency of hemorrhages as held earlier by Baratoux and later by Panse were not characteristic of lues. Furthermore, no one who has gone into the subject thoroughly has been able to corroborate the characteristic syphilitic vessel changes ventured by Baratoux.<sup>31</sup> The hemorrhages observed at odd times by all investigators were no doubt due, as claimed by Mayer, Asai, and Hofer, to either suffocation or postmortal effusion.

It would seem, furthermore, that in the majority of cases the meninges is the first attacked in the syphilitic process, the nerve next, and, if the case survives, eventually the inner ear. This is at least the order of involvement in the case of hereditary lues in the very young. That hereditary lues does attack the inner ear can hardly be doubted by any one who takes the time to study carefully the illustrations (70 to 79) in Panse's book on the Pathology of the Ear. The changes there represented can not be due to postmortal finding.

Concerning that large class of congenital syphilitics which develop deafness at a later period during the first or second decade, and occasionally later, and which manifest Hutchinson's well-known triad—diffuse corneal opacities, typically notched incisors and otherwise pegged teeth, and deafness—but little is known of its pathology because of the scarcity of the studied material. Mayer contends that the deafness is due to a recurrence or an exacerbation of the conditions which he found in the internal auditory canal of the syphilitic infants previously cited. In Logan Turner's case (quoted by Fraser) the diagnosis in spite of a negative Wassermann re-

action, was unquestionably syphilis, and with syphilitic evidence clear cut in both parents. After the death of the child, opportunity was offered to study the temporal bones microscopically. The middle and inner ear of both sides showed the same conditions—purulent otitis media with great thickening of submucous tissue; ankylosis of the head of the malleus to the outer attic wall; invasion of the marrow spaces surrounding the bony capsule of the labyrinth by a chronic form of osteomyelitis with numerous giant cells but no caseation; marked erosion of the bony labyrinth capsule by osteoelastic marrow; invasion of the semicircular canals by erosion of their bony walls and formation of granulation tissue in the perilymph spaces in such a way as to occlude the perilymph and endolymph spaces; marked dilatation of other parts of the membranous labyrinth, utricle, sacule and membranous cochlea. The two divisions of the eighth nerve, along with the facial, were normal. This case is not a fair illustration of primary internal ear involvement from inherited syphilis. It looks more like a case of bilateral labyrinthitis secondary to a middle ear suppuration with a sufficient element of syphilis in it to lower the general and local resistance and thus favor the extension of the suppuration to the internal ear.

In Downie's<sup>31</sup> case the patient died at eleven years of age of meningoencephalitis resulting from a fulminating gumma of the right parietal bone. The eighth nerve and the middle ear were normal. On the other hand, the semicircular canals were obliterated and the vestibule largely filled up with new bone formation. This case must be excluded as one of primary internal ear involvement since there was merely a macroscopic examination made. The case reported with illustrations of congenital syphilitic labyrinthitis by Panse<sup>27</sup> and referred to previously, is, no doubt, a *bona fide* case of labyrinthitis, but since he makes practically no mention of the nerve findings, we are left in doubt as to whether the case was one of primary affection of the labyrinth or one that might possibly have been due to extension from the eighth nerve.

Politzer,<sup>8</sup> in describing the anatomic changes in the inner ear, quotes Toynbee as having found thickening of the periosteum of the vestibule; Moos,<sup>32</sup> as having found thickening of the periosteum of the vestibule, the connective tissue between the membranous and osseous labyrinth infiltrated with small cells, hyperplastic, Corti's

organ and semicircular canals infiltrated with cells (presumably round cells) while the nerve was normal. This would seem to be a case of syphilis of the inner ear primarily and not due to an extension of the process from the nerve.

In a case observed by Politzer,<sup>5</sup> of a fifty-year-old man who had been deaf since his tenth year in consequence of a syphilitic affection and who died of phthisis, the histologic examination showed marked changes in the ganglion spirale. In its place were small round granular cells without distinct nuclei. There was atrophy and destruction of the ganglion cells in the ganglion spirale. In the spiral membrane, vestibule and semicircular canals there were no visible changes.

Oscar Beck,<sup>33</sup> noting the changes as the result of syphilis of the inner ear, mentions among other things an inflammation of the entire labyrinth, absence of the nerve fibers of the first cochlear whorl, new-formed bone and connective tissue, observed by Moos and Steinbruegge.<sup>34</sup> Bilateral complete destruction of the membranous labyrinth and the elements of both labyrinth windows together with new-formed fibrous and bone tissues have been observed by Gradenigo.<sup>35</sup> Rosenstein,<sup>36</sup> on the other hand, claims that not every case of hereditary luetic deafness cited by Gradenigo, can be proved to be a primary labyrinthitis, for it could be fundamentally a neuritis.

None of the textbooks—European or American—even the most recent ones, have much to say concerning the pathology of syphilis of the inner ear. Politzer starts his paragraph on the subject with, "The anatomic changes in labyrinth syphilis are but little known," and practically all others have followed in his footsteps, using the same or nearly the same expression. Most of the work in this field has been done by independent workers who have not yet entered the textbook class. Many of the textbook authors either confuse labyrinthitis with neuritis or else they have such a poor knack of arranging things that they leave the reader so confounded as not to be able to decipher the writer's meaning. For instance, in describing labyrinthitis the author will frequently start a paragraph dealing with the subject proper and later describes the changes in the eighth nerve. With few exceptions there is nothing to be found in the textbooks but a medley of thoughts without any intent at orderly arrangement. This lack of order I find in no less authoritative work

than that of Politzer,<sup>8</sup> Alexander,<sup>9</sup> Bezold,<sup>10</sup> and Panse,<sup>27</sup> not to mention a host of others by lesser lights.

Forgetting the textbooks at this time, since they afford so little information on the subject, and summarizing from the efforts of individual investigators in this field, we may safely conclude:

(1) That in the vast majority of cases of deafness from syphilis, the nerve is affected before the labyrinth.

(2) That the nerve may be affected to a slight or pronounced degree without the labyrinth becoming involved.

(3) That more often, however, the labyrinth does become involved along with the nerve, but to a less degree than the nerve.

(4) That in exceptional instances the labyrinth may become involved in a syphilitic process while the nerve escapes. Such findings, however, are not only rare, but the pathologic diagnosis has been questioned in some instances because of the carelessness of the investigator in depending entirely upon macroscopic findings, or in failing to report the nerve findings.

If the pathologic data on this subject is so meager as to leave doubt in some of the best minds, would it not be better for us to depend upon clinical methods if any exist in lieu of pathologic findings, or until such time as the question is definitely settled in the laboratory? If there is a satisfactory test, we should know more about it and make more common use of it in practice. I shall speak at greater length about this phase of the subject in a paper which is to appear later dealing with diagnosis.

A summary of the changes found in the labyrinth as the result of a syphilitic affection include hemorrhages, but not without question; congestion; round cell infiltration in the peri- and endolymphatic spaces; inflammatory exudates within the inner ear spaces; organized fibrous tissue and new-formed bone; aplasia and degeneration of Corti's organ and the cristæ ampullares; pus in the cavity of the inner ear; fixation of the footplate of the stapes; erosion of the labyrinth capsule associated with granulation tissue inside the cavity of the inner ear; malformation and arrested development of the osseous and membranous labyrinth or its contents; degeneration and aplasia of the ganglion spirale; atrophy of the delicate nerve fibers leading from Corti's organ to the ganglion spirale, obliteration of the labyrinthine spaces with bone; abnormally wide marrow spaces immediately surrounding the labyrinthine capsule.

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(To be continued)

## SYPHILIS OF THE EAR

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### ACQUIRED TYPE

**C**UTANEOUS Syphilis of the External Ear.—While it has long been recognized that syphilitic disease attacks every division of the auditory tract, from the auricle to the ultimate nuclei, the frequency with which this region is invaded is a point of great disagreement among observers. There are several reasons for this, but the chief one is, perhaps, that from the nature of the disease a primary lesion is not to be expected here, and hence is not recognized generally when it does occur. However, it may be stated definitely that, on the whole, primary syphilitic affections of the external ear are very rare. Thus, in the entire literature touching this especial subject, I have been able to find only thirty-two cases, of which at least twenty-five were "innocent" infections, such as those due to contact with an infected towel, the bite of an antagonist, etc. On the other hand, as a secondary manifestation, syphilis of the external ear is not uncommon, as the auricle and canal share the cutaneous invasion, especially in those cases where the face and scalp are involved. The skin lesion may be macular, papular or pustular; in fact, the pustular form is at times indistinguishable from this usually characteristic sign of variola. I once saw this mistake made, though it was one easily explained, as there was an epidemic of variola in the neighborhood. While gummata are rare in this region, they yield readily to constitutional treatment, but, when treatment is long delayed, are very destructive to the cartilage and leave deep, contracted scars (Buck, Hessler, Field, Politzer, West).

Primary sore of the meatus itself is most uncommon, for obvious reasons, and Sendriak reports the only two cases that the literature contains, in his review of it. The immunity from condylomata en-



joyed by the pinna is not shared by the meatus, as here they are found rather commonly, though nearly always easy of diagnosis, as they seem to appear chiefly as complications of other syphilitic lesions elsewhere in the body. The initial stage of infiltration and redness may easily escape notice, but as soon as the inflammation strikes into the cartilage, intense pain ensues, radiating over the side of the head, frequently accompanied by tinnitus and deafness. These grayish red, ragged, warty excrescences may heal by resolution or terminate in unhealthy, confluent ulcerations associated with an offensive purulent discharge. These ulcers are very resistant to treatment, requiring several weeks to several months to heal under constitutional treatment, which usually suffices as a therapeutic measure. Cicatrices may or may not result, though in their absence, there is permanent destruction of the hair follicles and secretory apparatus. Most observers agree that atresia of the canal generally does not occur, though I have twice seen this unfortunate result from neglect of treatment and failure to report for observation till the process had become deep-seated. It must, however, always be regarded as one of the possible complications, and proper precautions taken to prevent it. Local cleansing must be rigidly carried out, such as a preliminary wiping with peroxide, drying and keeping in constant contact with the denuded surface a wick impregnated with yellow oxide of mercury, or black wash. Frequent cauterization with lunar caustic or chromic acid will hasten healing.

Ulcerations of gummatous origin situated on the external ear are rare and occur seldom if ever in the absence of tertiary lesions elsewhere in the body. Indeed, the diagnosis rests almost solely on this corroborative evidence and on the effect of specific treatment, as they are lacking in such characteristics as would warrant a definite diagnosis without further signs. Instances are not common in the literature, but where found they are generally described as having flattened, fatty bases with steep, elevated margins, sharply demarked from the surrounding parts. Specific treatment combined with local cleansing and dusting with mercurial powders generally establishes a firmly healed site, though cauterization at times is indicated when the lesion appears sluggish. Were the drum exposed to easy inspection, its involvement would probably be noted more frequently in printed reports. This fact, together with the

additional one, that syphilis is generally treated by an attendant not gifted in examination of the ear, or especially interested in its behavior, perhaps accounts for the paucity of recorded cases. Moreover, it is well to remember that the canal is frequently occluded by the same process that may be causing the drum lesion, thus effectually preventing such inspection as the examiner might be eager to make. I find but three cases recorded (Lang, Baratoux, Ravogli).

*Syphilitic Infection of Eustachian Tube and Middle Ear.*—The reports of the past twenty-five years so seldom mention syphilitic infection of the tube as a primary lesion, that it seems hardly necessary to dwell on this complication, though in the early reports this infection, chiefly through use of an infected catheter, was accomplished oftener than it is pleasant to contemplate. Despite the casual mention of Politzer and Dalby, who record its rare occurrence, West considers that there have been more cases than the very considerable number actually reported. This speaks eloquently of the lack of ordinary cleanliness (much less of actual asepsis) and of careful, gentle catheterization, since mere contact would not usually cause infection. West has gathered reports of ninety-five cases, as published by Burow, Sendriak, and Lancereaux, the last of whom is not sure of the specific nature of the case he reports.

As might be supposed from a knowledge of the histology of the part and the all-pervading nature of the syphilitic poison, infection of the middle ear occurs in all degrees and in all three stages of the disease, in which an extension through the tube is the most easily understood means, when such a tubal lesion exists. Where this causes a catarrhal swelling and tumefaction of the tube, the clinical picture in the middle ear is no different from that of a simple infection, such as a retraction of the drum, which is congested, reduced hearing and possibly a negative Rinné. In early syphilis one of the most constant signs is reduced bone conduction, but this is so important a point that it will be discussed at length later on. It can be stated positively that there is no characteristic appearance of the drum, or any definite clinical aspect in a case under the foregoing circumstances. If inflation does not give immediate relief, then we have to deal with something beyond the middle ear: infection of the labyrinth, with or without syphilis of the central nervous system. While it is not susceptible of proof, and is somewhat a matter

of academic interest, it seems reasonable to suppose that the mucosa of the tympanum is subject to the eruptive conditions found elsewhere in the secondary stage. Here the infection may be of the catarrhal, adhesive catarrhal or suppurative type (Politzer), but, again, there is no typical picture to justify the diagnosis of syphilitic origin, as this can be established only after the rapid destruction of the membrana tympani and the marked shortening of the bone conduction. The occurrence of a simple suppurative otitis media complicating a syphilitic infection is not infrequent, but the course of the suppuration is relatively so much less malignant and the effect of specific treatment so little evident in the ear condition that the differential diagnosis soon becomes apparent. The appearance of tinnitus, vertigo, or severe loss of hearing should suggest a deeper invasion than that of the middle ear, though both may coexist. All the foregoing conditions are readily submissive to energetic, early treatment in most cases, but when delay has allowed destruction in part or entirely of the drum, ossicles or any part of the tympanic walls, the prognosis is bad; in fact, Bell's palsy is one of the likely results.

The responsibility of tertiary syphilis for any suppuration in the middle ear is even more difficult to establish than that of the secondary period, yet when it does occur the destructive changes are rapid and extensive. The ravages of an untreated tertiary syphilis when once established in a bony nidus would lead to the natural expectation that a brain abscess would complicate a suppurative middle ear condition where the tympanic walls were necrosed and even the petrous portion of the temporal bone eroded, yet such is rarely the case. Baumann's case, for example, went to operation for mastoid abscess, there being polypi and small sequestra in the middle ear, but the wound remained open till iodide of potash was administered, yet no brain complication was seen. While invasion of the cranial cavity is not usual, yet erosion of the wall of the lateral sinus and of the carotid artery has occurred with great loss of blood (Hessler). Pollak was the first to describe gummata of the mastoid process, which occur at times independently of any aural symptoms (Pollak, Collet and Beuter). West reports four cases in which there was no history of syphilis, but the exhibition of specific treatment quickly caused a disappearance of the mass and established its nature. This

latter point was totally obscure, and three of the cases were in many ways most anomalous.

*Syphilis of the Internal Ear.*—Auditory disturbances of syphilitic origin usually appear in the late secondary or early tertiary period, though Politzer reports two cases which show the wide range within which hearing may be affected after exposure. The first had distinct acoustic symptoms seven days after the appearance of the chancre, and the other had no such symptoms till the lapse of twenty-one years, when a gumma of the head appeared. Again, disturbances in the hearing function may appear without any other syphilitic manifestation whatever. Nowhere does syphilis show its protean, elusive, unexpected and confounding characteristics more than in its insidious attack on the internal ear. This condition of baffling obscurity, its dire effect on the hearing of the patient with all that this loss spells in social and economic disaster combine to render this division of aural syphilis the most absorbing to the investigator, and the most important to him and humanity.

Owing to the insidious nature of the infection and to the usually somewhat casual nature of the aural examination (if, indeed, any be made at all), this complication, as before remarked, has escaped record very often; so the frequency with which auditory disturbances complicate constitutional syphilis can not be estimated with any satisfactory degree of accuracy. Thus, Politzer accepts the vague statement that from 7 to 48 per cent show aural lesions (Schwabach, Kretschmann, Wiese,<sup>9</sup> p. 754), which, in justice to him, is the view that is generally held, though it is hardly better than no estimate at all. With West, I believe that 5 per cent is sufficiently near the proper proportion to serve as a guide in study and investigation. Certainly 48 per cent is much too high a percentage in America. Whatever the true estimate may be, the wide difference of opinion on this subject is an evidence of the unsatisfactory condition of the history and records of such cases. There is another aspect of these cases which offers a more easily ascertained incidence, for it seems nearly certain that about 50 per cent of all aural lesions that do occur in aural syphilis make themselves manifest in the secondary period, and, accordingly, they should be searched for in this stage.

The early writers were almost a unit in their conviction that the

labyrinth was the part affected in syphilitic disease of the internal ear, and Habermann and Kreibich wrote so convincingly, and the weight of their influence was so great that this belief was well-nigh universal for a while. However, of those to dissent, Gradenigo was the first to attempt any systematic differential diagnosis, and rather leaned to the belief that the lesion was oftener one of the nerve trunk, though he admits that a clinical differentiation presents one of the most difficult of problems. On the other hand, Rosenstein makes the rather oracular statement that only rarely is the lesion labyrinthine, but Nonne puts his finger on one of the most significant and important facts, hitherto apparently either unknown or regarded as negligible, when he comments on the coincidence that frequently disturbances of the acoustic nerve are associated with similar disturbances of other cranial nerves. This observation paves the way to the recognition of the revolutionizing nature of the statement of Swift and Ellis, who have shown rather convincingly that sudden deafness in the presence of syphilis is rarely due to any infection of the eighth nerve, or labyrinth, alone, but is generally a manifestation of that very serious disease, syphilis of the central nervous system, of which more will be said later. In his review of the literature, Benario seems to prove that the eighth nerve is oftener affected in early syphilis than any other cranial nerve (Habermann, Mayer, Rigaud, Politzer, Rozier). Nonne further observes that in his opinion the involvement of the eighth nerve is associated with a basal meningitis, a fact that is emphasized by Swift and Ellis, though they state the matter somewhat differently, adding that this is demonstrable by lumbar puncture. Knick and Zaloziecki are credited with precedence (1911) in their demonstration of a definite change in the spinal fluid in the presence of syphilitic disease of the eighth nerve. This change, viewed in the light of the symptoms, seems to establish the clinical fact that in the early cases of auditory disturbances, and perhaps in the late as well, such disturbances are due to an involvement of the eighth nerve in the course of a syphilitic meningitis.

Glogau, observing that many cases of *tabes dorsalis* showed impaired hearing, made careful tests and found that from 40 to 50 per cent were suffering from impaired or complete loss of hearing in one or even both ears, and also shortened or complete loss of bone

conduction. Swift and Ellis<sup>17</sup> urge that the sudden deafness of the syphilitic be regarded not merely as isolated disease of the eighth nerve or labyrinth, but as an incident in the course of syphilitic disease of the central nervous system. The prognosis of syphilitic deafness, notoriously bad, has been greatly improved by their method of intraspinal injections of salvarsanized serum. In early cases many have been completely cured of marked impairment of hearing.

Sudden loss of hearing, generally with tinnitus, no pain, no evidence of middle ear disease, in a young adult otherwise healthy should be regarded as almost certainly indicative of syphilitic disease of the eighth nerve and labyrinth. The high-toned forks will be those least appreciable, and the watch, acoumeter and Galton whistle will elicit little, if any, response, yet conversation may be heard. However, in the marked shortening of bone conduction we have one of the most striking and reliable evidences of luetic infection, as it is perhaps the most constant sign, occurring in 95 per cent of the cases. A deafness without apparent middle ear trouble showing a positive Rinne should at once arrest the attention of any aurist. In the presence of other signs of syphilis, the diagnosis will present no difficulties, but in their absence, it is not usually easy. As a rule both ears are involved, though one may be so much the worse that the other may appear normal, but this deception soon becomes evident, as the deafness is rapidly progressive, and the bilateral nature of the trouble is soon disclosed. Therapeutic means of diagnosis, useful elsewhere, are practically useless here, as syphilitic deafness is notably intractable, though the Swift-Ellis treatment is an exception to this rule, and may prove diagnostic as well as curative. No assistance in diagnosis is lent by the appearance of the drum, as it is not affected in any characteristic way; whereas a coincident suppurative condition, or a preexisting catarrhal condition of the tympanum may actually obscure the etiology. Either condition will demand consideration where it coexists with a syphilitic process. Inflation will not improve the hearing except in the presence of some tubal or catarrhal complication, and may even increase it. Facial palsy is a rare complication and occurs occasionally in the secondary stage associated with labyrinthine syphilis, and practically never in the third period (Lannois).

Our knowledge of the morbid anatomy is most limited and comprises the observations of a few cases at the hands of so few aurists that it is not safe to base any broad statements on their findings. However, from what has been reported of the changes in the secondary stage it would seem that hyperemia of the membranous labyrinth and increased perilymphatic pressure are to be expected; later, a small-celled infiltration and degeneration of the end-epithelium in the cochlea and ampullary crests (West). In addition to these conditions Voltolini (quoted by West) found in one case of secondary syphilis circumscribed hyperostosis around the fenestra ovalis (Moos). Moos's case showed about the same condition, but is particularly interesting as demonstrating that it is possible to have a true labyrinthitis and the nerve trunk remain normal. Moos and Steinbrugge report a case which perhaps best summarizes the morbid anatomy in the tertiary stage. They found these conditions: enlargement of the osseous spaces in the temporal bone and in the labyrinthine capsule, enlarged marrow spaces filled with fibrous tissue, itself infiltrated with small cells and adherent to the periosteum of the labyrinthine wall in several places, bloody extravasation between the fibers of the acoustic nerve and in the cochlea, and degeneration of the ganglionic layer in Rosenthal's canal (quoted by Politzer).

#### CONGENITAL TYPE

West's division into three groups of inherited syphilitic disease of the ear is a rational method for study, as the clinical features are so different in each of the three, and occur at such widely different ages. This is his classification: (1) Cases showing gross aural disease at birth; (2) cases showing aural disease shortly after birth; (3) cases showing aural disease at or after adolescence, or much later (i. e., all cases not included in 1 and 2).

Of the lesions of the external ear, seemingly due to inherited syphilis, I have seen three cases of microtia. Fortunately for society and for their own happiness most of the children showing gross syphilitic disease of the ear die shortly after birth, but in those less frequent cases where they survive, they become not only deaf mutes, but often mental defectives as well. Of these three the first died at six weeks of age. He showed almost complete absence of pinnae,

and the mastoid process was entirely absent, the face shrunken and prematurely old in appearance. There was a vertical series of fibriated remnants where nature had intended a pinna to grow, no canal and apparently no acoustic development at all. The second was a boy of twelve, whose left head showed a striking lack of development, which included the pinna, a mere fringe, and no canal. Where the mastoid should have been was a vertical scar, the site of an operation to restore the function of hearing, but the venturesome surgeon desisted when he found no bony canal. The asymmetry extended as far as the parietal bone, whose eminence was totally lacking, and the bulge of the frontal bone also. The third case, also unilateral, was that of a man of thirty-five, the general aspects of the case being the same as the second. All three had definite syphilitic histories on the father's side. In such obviously syphilitic cases, the diagnosis presents no especial difficulty, but in the second group we have to depend on the appearance of Hutchinson teeth, which are found in 50 per cent of the cases (Fraser), a persistent nasal discharge, stubborn middle ear suppuration, interstitial keratitis, defects of the hard and soft palate, marked deafness without discharge from the middle ear. The stunted appearance, lack of vitality, pallor, appearance of premature age seen in children from 3 to 6 years of age constitute strong presumptive evidence of inherited syphilis. Recourse must be had to the Wassermann test in all doubtful cases, and is a prudent measure in all cases as it may be highly desirable to have some strong corroborative proof with which to confront parents who are often resentful of such a diagnosis without proof, whatever may be their own knowledge of culpability. The hopeless nature of the prognosis in those labyrinthine cases, is easily grasped in a perusal of Baratoux's investigations. Of forty-three cases reviewed nineteen were stillborn, but of the surviving twenty-four eight had chronic suppurative otitis media, three isolated labyrinthine disease, and eight both middle ear and labyrinthine disease. The labyrinthine cases showed either suppuration therein or hemorrhage and destruction of Corti's organ. The suppuration in this second group may be nonspecific in rare instances, but even so, its course is necessarily affected by the lowered vitality, and rapid destruction of the drum and tympanic contents is apt to ensue, even the internal ear being penetrated by



the suppurative process in extreme cases. Rarely condylomata occur (Grueber, Schwartze, Buck, Knapp,<sup>84</sup> p. 274) and the skin eruption on the pinna and in the canal may be in any of its forms (Habermann,<sup>84</sup> p. 274). I have once seen the macular form, spread over the pinna and face, in a stillborn infant.

The frequently encountered type of congenital aural disease is that of the adult and of late life. According to West, the proportion of hereditary syphilitics who have deafness and other aural manifestations of syphilis is thus stated by various observers: Hutchinson and Jackson, 10 per cent; Hermet and Baratoux, 30 per cent; (Politzer); Habermann, 20 to 66 per cent; Alt, 3.1 per cent (labyrinthine deafness); Hinton, 5 per cent (all seen at Guy's Hospital, all quoted by Nonne,<sup>84</sup> p. 275). There is a little closer agreement than this among the authorities as to age limits, eight to eighteen years being the general estimate, or in the neighborhood of fourteen (Knapp).

In the appearance of interstitial keratitis we have presented to us not only a diagnosis of the aural condition impending, or actually active, but a warning as well, that treatment started at this time will heal in part any aural lesion, but also energetically persisted in, will probably prevent those parasymphilitic lesions, which are so destructive to the health and economic value of the patient, and even to life itself. The keratitis nearly always precedes by weeks or days the ear lesion, though it may develop simultaneously with it. The estimates as to the preponderance of females over males in congenital syphilitic deafness vary from 2 to 1 (Hutchinson, Gradenigo) to 4 to 1 (Pierce). As the symptoms of adult congenital syphilis of the ear are almost the same as those of acquired syphilitic labyrinthitis, there is no need to repeat them here.

#### TREATMENT

The introduction of salvarsan ("606") was so enthusiastically exploited that its virtues were much exaggerated, even beyond what Ehrlich himself believed it capable of accomplishing. A single dose of this highly efficient remedy may have permanently cured a syphilitic infection, though it is exceedingly unlikely, and I believe that no case was ever so fortunate. However, such claims are occasionally made. When the indications are as set forth already

in this treatise, indicating syphilis of the central nervous system, the Swift-Ellis treatment<sup>17</sup> is the only one that will give thorough access to the syphilitic toxin and should be given strictly as laid down by those two observers (see also, Robertson, A. R.<sup>18</sup>). With this exception, the routine treatment should be that which Kerrison says is the outgrowth of Fordyce's vast experience as a syphilographer, and this is as follows: a preliminary dose of 0.3 gm. to a woman, or 0.4 gm. to a man, intravenously, as a test of such idiosyncrasy as may exist for the remedy. If no contraindications prove to exist, a week later an injection of 0.4 gm. or 0.5 gm. (woman or man) is given. Thus, five or six are given at weekly intervals, followed by a thorough course of mercurial inunctions, or injections. A period of rest next ensues for six weeks or so, if the case is an early one and the symptoms have been well controlled; at the end of this time a Wassermann test is made. If this proves positive, the whole procedure is repeated till a negative result is obtained.

It has been insisted that the use of this remedy has increased the nerve lesions, and I have reported a case that seemed certainly an arsenic neuritis. However, many observers of note deny this, and the controversy is well discussed in all its aspects by Benario, J., Duel, A. B., Alexander, Finger, and many others.

The treatment of all stages is the same, and local lesions are to be treated as already indicated, or otherwise appropriately as they would be in a nonsyphilitic subject. The Swift-Ellis method should always be kept in mind where keratitis and sudden deafness arise, and a lumbar puncture done to determine the presence of the pathognomonic change in the spinal fluid.

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## SYPHILIS AND MALIGNANCY

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**B**OTH syphilis and malignant disease are on the increase, and since the lesions of one are not infrequently mistaken for the other, the study of any relationship that may exist between them is of absorbing interest, not only to the syphilologist, but to the surgeon as well. The cause of syphilis we know; the cause of cancer is still a mystery. The two diseases have been observed for many centuries and the pathology and clinical phenomena of each are well defined, yet there is a strange borderline where the two conditions seem to meet and merge, wherein are secrets still unsolved. It is our purpose, therefore, in this communication to examine the facts and correlate them in so far as syphilis is concerned as a causative agent in the production of malignant growths.

The oldest view concerning the relation between cancer and lues was that they were mutually antagonistic to each other and that a syphilitic was more or less immune to cancer. This at once brings to the front the opposite proposition: Does syphilis increase the predisposition to malignant disease? As far back as 1843, Leroy d'Etiolles stated that one syphilitic out of twenty-five developed carcinoma. In 1884, Ozenne advocated the theory that syphilis determined the point of least resistance for the appearance of carcinoma. In 1907, Horand in an extensive review repeated the argument and cited many examples. In 1888, Cozzolino produced evidence of a conclusive nature that cancer developed rapidly on a background of early syphilis and more slowly on late syphilis. He also stated that when cancer appeared on what had formerly been a syphilitic lesion, it was accompanied with a relapse of the luetic infection. Esmarch, and also Wasmer, advanced the postulate that because of the tendency of syphilis to attack connective tissue, the presence of lues would favor the development of sarcoma rather than carcinoma. In a paper published in France just before the war, Poirier reported thirty-two cases of malignant disease of the tongue

in which twenty-seven were syphilitic. The German surgeon, Diefenbach, was so thoroughly convinced of the fact that malignancy follows syphilis that after every operation for the removal or amelioration of a cancerous growth he instituted a course of mercurial inunctions.

It is well known clinically that carcinoma or epithelioma not infrequently occurs on the site of a healed syphilitic scar. But it must also be remembered that cancer occurs with equal frequency on scars which were not of syphilitic origin. So eminent an observer as Jonathan Hutchinson stated that he had often seen a malignant growth developed on a healed syphilitic lesion. Czerny and Caan, in the Heidelberg Cancer Institute, took a Wassermann of all cancer patients admitted thereto and were surprised to note the frequency of positive reactions. Salvarsan had no effect in so far as carcinoma or epithelioma was concerned, but with sarcomatous growths they sometimes obtained favorable results. It has also been observed in the so-called Dithmar's disease, which we now know to be a form of inveterate hereditary syphilis, that many of those affected later developed malignant disease.

In 168 case histories reported by Horand, the majority refer to cancer of the mouth or tongue. Nearly all of them had leucoplakia lingualis or buccalis previous to the development of malignancy. Fournier asserts that leucoplakia is invariably syphilitic, and Berenger, Kopp, Kaposi, Landinzy and Gaucher also regard syphilis as the sole cause of leucoplakia. Fournier further states that many of these cases of leucoplakia later become malignant. In support of this statement he cites the analysis of 184 cases of buccal cancer following leucoplakia in which 84 per cent were known to have had syphilis. I have already mentioned Poirier's series of cancer of the tongue of which 27 out of 32 were syphilitic. It must be admitted that such frequent occurrences could hardly be due to coincidence. I desire to call the reader's attention, however, to the fact that these cases occurred almost entirely in males, and many of them gave a history of prolonged and excessive use of tobacco, so that a diagnosis of smoker's cancer would not be entirely out of place. The French dermatologist, Brault, writing in 1898, claimed that in epithelioma of the tongue there was almost always a history of syphilis in youth. This was before the days of the Wassermann and it is quite possible

that Brault was mistaken in the diagnosis of some of his cases of epithelioma which were really syphilis.

In the series reported by Horand he notes that 40 of them were of a hybrid type; i. e., cancer and syphilis were present in the same lesion. He calls them juxtasymphilitic cancer. His case L illustrates this condition very well. A man of thirty-eight had an infiltrated ulcer of the lower lip which had persisted for a long time, but which yielded promptly to potassium iodide. After two years the ulcer returned, when it was found to be cancer in part; i. e., syphiloma with cancer nests. I am reminded of a similar case brought to my attention at autopsy, in which there were lesions on the buccal and lingual surfaces and larynx that were patently syphilitic, yet histologic examination demonstrated that a transformation into epithelioma was taking place. Cases such as these are not uncommon, but, as Horand wrote before the discovery of the *spirochete pallidum* and the Wassermann reaction, it is quite possible that the knowledge we now possess would, in some instances, have modified his diagnosis. Similar cases of malignant growths grafted upon gummata have been reported by Jaboulay, by Montgomery and Sherman, and by Rohrbach, pathologist in the University of Breslau. I am of the opinion that they represent a true clinical entity and Horand and Fournier were undoubtedly right in diagnosing some of them as hybrids—carcinoma or epithelioma coexistent with syphiloma in the same lesion.

As the penis is the most frequent site of chancre, it is of interest to note the number of malignant growths originating from that organ in which there was a previous history of syphilis. In 1877, Demarquay collected one hundred and thirty-four cases from the literature and from personal experience. In fifty-nine of these, syphilis is given as the cause. His paper is somewhat lacking in detail, but the inference he draws is that chancre, chancre redux and gummata have a tendency to cause cancer. In an analysis by Downey of one hundred cases of epithelioma of the penis occurring in the Massachusetts General Hospital from 1872 to 1905, he notes that in two, the cancer appeared on the site of the chancre after a lapse of twenty-two and thirty years, respectively. Martin and Sibley also report having seen a cancer develop on the former site of a chancre.

I recently saw a cancer of the penis removed by Professor Chet-



wood of the New York Polyclinic Hospital, in a patient of middle age who gave a history of having had a chancre twenty years before. The Wassermann was strongly positive in spite of vigorous treatment with novarsenobenzol and mercury.

King, of Kansas City, writing in 1898, described a number of cases of syphilis which had apparently been contracted from individuals suffering with cancer. It so happened that nearly all of the victims of the syphilitic infection were surgeons who had contracted digital chancres while operating on cancer. In none of them was there any doubt of the diagnosis of syphilis or of the manner of the infection, nor was there any doubt as to the diagnosis of cancer in the patients operated upon. King, however, fails to state whether any of these cancerous patients showed any of the clinical signs of lues. Also he wrote before the discovery of the *spirochete pallidum* and the Wassermann reaction and his method of bacteriologic expression, if I may be allowed to use that term, is not altogether in accord with modern ideas. Yet, however we may speculate, the fact remains that four physicians were inoculated with syphilis while operating on cancer; which proves at least, that these four cancer cases were also actively syphilitic.

Coming nearer to the present and within the period of the Wassermann and the *spirochete pallidum*, let us consider the two diseases from the angle with which they have been studied by O'Day—the exact simulation of cancer by syphilis. O'Day describes a case which may be taken as typical: A woman of forty-eight, who had been examined by a number of competent men who diagnosed her condition as cancer of the cervix. The odor characteristic of uterine cancer was present and she had metrorrhagia to an extent to render her extremely anemic. She was cachectic and also had bedsores. Suddenly mucous patches appeared. A Wassermann was taken which was found to be strongly positive. Under antisyphilitic treatment the patient recovered. O'Day enumerates several other cases of supposed malignancy which in reality were syphilis; one that had been diagnosed as cancer of the stomach, another of an intraabdominal growth and one of a growth involving the orbit.

I have no hesitancy in saying that I believe syphilis to be a factor—a very potent factor—in the causation of malignancy. In this opinion it will be seen that I am not alone. Especially is this true

in regard to buccal and lingual cancers which form a not inconsiderable percentage of malignant disease. I believe that this causal relation exists between them because syphilis produces a *locus minoris resistentia* that renders the tissues more susceptible to the development of aberrant cells. I am also of the opinion that in every case of supposed malignancy, careful exclusion of syphilis should be made.

In conclusion I desire to attract the reader's attention to the following facts which I have endeavored to substantiate by typical and convincing examples.

I. Syphilis predisposes to malignant disease.

II. The most malignant forms of syphilis and cancer may exist side by side—the so-called juxtasyphilitic carcinoma or epithelioma.

III. In a syphilitic developing cancer there is almost certain to be a local outbreak of the luetic disease in close proximity to the malignant growth.

IV. In an individual with cancer who contracts syphilis, the malignant disease is stimulated to increased activity.

V. Leucoplakia occurring in syphilitics, especially if tobacco is used to excess, almost invariably develop cancer of the mouth or tongue.

VI. Epithelioma or carcinoma may develop on a gumma, the two lesions merging, as it were.

VII. Syphilis may exactly simulate cancer in any location, either of the viscera or on the surface of the body.

## SYPHILITIC AORTITIS

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THE cardiovascular manifestations of syphilis are so important that it is doubtful whether they should rank in point of gravity below the lesions of the central nervous system. So much attention has been given to syphilitic disease of the central nervous system that general interest in the cardiovascular manifestations of syphilis has not always been sustained. The relationship between syphilis and disease of the cardiovascular system has long been known. Since the time that Morgagni called attention to the role of syphilis in the etiology of aneurysm, considerable literature has sprung up.

There are two important reasons why any contribution to this subject is of value: First, the widespread incidence of these conditions, and, secondly, the fact that a more general interest in their existence might stimulate a search for the earliest manifestations at a time when treatment would be of real value.

It is very difficult to determine the exact role of syphilis in the causation of cardiovascular disease. This question of frequency may be approached from various aspects. It is obviously true that a higher percentage of incidence will be found from the standpoint of the pathologist at autopsy.

Many of the cases of cardiovascular syphilis which are revealed at autopsy by pathologic or bacteriologic study have been latent or unrecognized during life. Careful study during life will render it possible to recognize most of the moderately well advanced cases of aortitis due to syphilis, but there is a considerable percentage of error. One of the most important elements of error is the fact that nonspecific cardiovascular disease may be present in a syphilitic. There are also without doubt cases of mixed infection.

Mussey states that in 1379 cases of syphilis, there was clear cut syphilitic disease of the heart or aorta in 59 (4.2 per cent). This

percentage is in striking contrast to the statement of Oberndorfer that syphilitic aortitis was found in 82 per cent of the autopsies done on individuals with acquired syphilis. This means that cardiovascular manifestations are practically universal in syphilis. It is to be expected, however, that the early and intensive treatment of the present day will show a reduction in this high figure. In the series of 251 heart cases studied by Koreyznski, syphilis was determined in 22 per cent.

#### THE SERIES HERE STUDIED

The cases here analyzed consisted of 215 patients with syphilis in all stages. These patients are considered from a clinical point of view only. No pathologic studies have been made, inasmuch as this series was in private practice, and all but four patients are living so far as known. Out of the 215 cases, there was a clinical diagnosis of aortitis or allied conditions in 24 instances (11.1 per cent). These patients have all been seen during a period beginning three years ago, and running up to the present time. Patients who have been seen one time only are not included, nor have those been included who have been watched insufficiently to draw definite clinical conclusions. I have treated all of these patients for various periods of time. In this way the series of cases is in reality a consecutive one, with the exception of the patients seen but one time or under circumstances of unsatisfactory observations. The patients seen have included all types of syphilis from early chancre to late stages.

The data on which a clinical diagnosis of aortitis has been made is considered later in the text. The diagnoses are based on carefully taken histories, physical examination, Wassermann reactions, and the x-ray findings.\* It is, of course, apparent that anatomic studies would show a greater incidence of aortitis than clinical diagnoses. The true incidence of syphilitic aortitis is, therefore, a high one.

The classification of cases is as follows:

Aortitis,	9
Aortitis with marked dilatation,	5
Aortitis with aortic insufficiency,	7
Aneurysm,	3
	<hr/>
Total,	24

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\*The x-ray examinations have been made by my associate, Dr. J. T. Murphy.

The ages of these patients were as follows:

Age 20-30 years,	5
“ 31-40 “	7
“ 41-50 “	8
“ 51-60 “	3
“ 60 and over,	1
	<hr/> 24

The cardiovascular lesions of syphilis occur at an early period of adult life. Perhaps most cases of aortitis give rise to trouble between the ages of 40 and 50. Over one-half of Longcope's cases were under 40. It is not rare to meet with cases in the twenties.

#### THE WASSERMANN REACTION

It was not until the application of the Wassermann reaction became general that interest in cardiovascular syphilis was widespread. The results of the Wassermann reaction applied in a clinical way approached so closely the results of pathologic studies, that doubt could no longer persist that syphilis was a decided factor in the causation of heart and aortic disease. The Wassermann reaction is positive in from 75 to 80 per cent of the cases which show syphilitic changes in the aorta at autopsy. Collective statistics will show a slightly smaller percentage, 70 to 75 per cent of positive Wassermans in cases of frank syphilitic cardiac or aortic disease.

The Wassermann reaction was made in all of the cases herein considered. Eighteen of the twenty-four gave positive reactions (75 per cent). Of the six patients with negative Wassermann reactions, there were two with signs of unquestionable tabes, such as fixed pupils, absent knee-jerks, and ataxia. Neither of these two patients had lumbar puncture performed. Two other patients gave very clear histories of having, and being treated for syphilis. Another gave no history, but had a sharply punched out ulceration over the shin of one leg, which immediately cleared up after two injections of diarsenol. The sixth patient with a negative Wassermann gave a negative history, but showed on examination a perforated nasal septum and a scar on the neck under the ear, which had followed a long-standing skin lesion at this place.

The discovery of the spirochetes in the heart muscle and aorta affords final and convincing proof of the relation between syphilis

and the disease under consideration. The presence of spirochetes in the tissues does not, however, rule out all other factors.

#### INTERVAL BETWEEN THE INFECTION AND THE DISEASE

The importance of this interval is at once apparent. It is indeed an interval of safety. It is not possible in a given case to determine the exact duration of this period. It is certainly very variable. A clear distinction should be made between the time of actual infection of the aorta and the time when symptoms or signs can be demonstrated. It is very probable that there is a latent period in all cases, although certain reported cases show how short it may be. Inasmuch as the time between the primary infection and the general invasion of the blood is very short, it is probable that the first involvement of the aorta occurs very early in the disease. Indeed, the aorta seems to be one of the sites of predilection for early infection. It is not proved, however, that this infection is the sole cause of the cardiac symptoms so often appearing in the primary and secondary stages of syphilis. Palpitation, arrhythmia, tachycardia, and pulse disturbance are mentioned by Fournier, Grassman, Longcope, and many others.

The series of cases studied by Grassman showed arrhythmia or pulse disturbances in 85 per cent of 288 patients with secondary syphilis. His further findings that 40 per cent of these same patients showed heart murmurs, most often from dilatation, is striking. It is at once apparent that functional heart disturbances are to be expected in the early course of syphilis. The shock of discovery, often the despair of realization, may well bring about profound functional disturbances in the nervous system. Such functional disturbances in the nervous system are often manifested in cardiac symptoms, but can not bring on dilatation of the heart with the high incidence of murmurs mentioned by Grassman.

There have been a number of instances cited in the literature where definite organic aortic disease was present within a few months after the primary infection. Admitting the existence of such early cases, it is undoubtedly true that they are exceptional. The ever recurring possibility that a given case may be congenital adds to the difficulty of determining the early involvement. The term involvement is here used in the sense of clinical discovery. In Koreczynski's series of 251 heart cases, the shortest interval between

infection and aortic involvement was three years, with an average interval between fifteen and thirty years. Elliott states that five years is the average interval. Instances are reported, such as the case of Grau, where the involvement is long delayed, even for forty or fifty years.

It is unfortunately true that serious damage may have taken place in the heart or aorta before the patient is conscious of having serious disturbance. This fact should serve to throw the burden of responsibility on the physician, who by his knowledge of the frequency of such disease, should search for it, rather than have it thrust upon him.

An attempt was made to determine the time which had elapsed between the beginning of infection and the onset of the cardiovascular manifestations. It was not always possible to do this. Of the twenty-four patients, seven had no knowledge of having acquired syphilis, or at least denied such knowledge. In two other patients there was a history of having sores at various times prior to the beginning of the present trouble. It was not possible to state in either of these patients, which of the several sores was the actual initial lesion. In sixteen patients, a definite date was determined as the beginning of the syphilis. One of these showed cardiovascular manifestations two years after his initial infection. This was the shortest period of latency observed in any of the twenty-four patients. This case was that of a man thirty-four years old admitting a venereal lesion two years before. The lesion was treated with the application of some local agent by his physician at the time. He was also given some internal medication containing iodides for a period of eight weeks after the lesion was healed. No skin lesions were noted at any time. When I saw him, he had a four plus Wassermann reaction, an irritating cough, sputum, dyspnea on exertion, and considerable pain under sternum when he coughed. There was no pain when not coughing. Examination showed a distinct systolic bruit over the second and third interspaces of the right side. The second aortic tone was loud, both relatively and absolutely. Blood pressure 165-95. This patient was put on specific treatment with entire relief of his cough and pain. The murmur persists as before.

The longest interval before the onset of symptoms was in the case of a patient who developed dyspnea twenty-seven years after his infection. It is very difficult to determine the exact onset of the

symptoms. Patients with syphilis, especially of the better class, are apt to be introspective, and self-analytic. Vague pains in the chest are commonly admitted, if the questioning is careful, and it may not be possible to differentiate such pains from those having an organic basis.

#### ANATOMIC CHANGES

The parts of the aorta most commonly affected are the root and the arch. This localization may be due to the greater functional strain borne by the first part of the aorta on receipt of the impact of the mass of blood thrown out at each beat of the left ventricle. The explanation of Klotz is that the relationship of the lymphatics to the first part of the aorta determines the involvement. The lymphatics are more widely distributed in the first part of the aorta than lower down in its course. Inasmuch as the infection in syphilis follows the course of the vasa vasorum, a perivascular infiltration can be demonstrated in aortitis. The lymphatics are probably more important than the small blood vessels in the localization of specific changes in the first portion and arch of the aorta.

From its usual localization at the root of the aorta just above the semilunar valves, the pathologic process tends to advance along the arch, and also downward to the valves. Green states that the line of march from the initial point to the valve flaps is characteristic and that in 80 per cent of the cases secondary aortitic regurgitation results. It is not true, however, that the first part and the arch of the aorta are the only parts involved. There may be involvement of the thoracic and abdominal aorta also, and at times exclusively so. There appears to be a greater predilection for involvement of the abdominal aorta at the site of the coeliac axis.

The gross anatomic changes take a variable form. The coronary arteries may be partially or completely obstructed at their openings although the pathologic involvement does not usually extend far along the course of the vessels. The large branches of the aorta, the innominate and left carotid, may be involved by obstruction or by dilatation. Aneurysmal sacs of variable size may develop, or dilatation of variable type may ensue. An aortitis may exist for many years, even indefinitely, without involving the aortic ring and the valve flaps. When this has taken place, the condition becomes at once more serious, and may indeed be said to mark the beginning



of the end. The localization of the disease is, therefore, more important than the extent. Widespread aortitis may be consistent with absolute latency so far as clinical manifestations are concerned.

#### HISTOLOGIC CHANGES

It is probable that syphilis invades the aorta by way of the vasa vasorum. This network is most pronounced in the adventitia and immediately under, and it is here that changes are first detected. The media becomes thickened following the adventitia. With the naked eye, changes can be detected from within sooner than from without. The plaques are at first small, sharply demarcated, pale, hyaline, elevated, variable in size, smooth, and elastic in consistence. Later the patches become larger, more irregular, and may merge with others. In advanced instances, the inner wall of the aorta looks scarred, pitted, wrinkled, showing yellowish gray patches. Calcification is absent except in very advanced cases. The tendency to dilatation is due to the fact that the vessel wall undergoes corrosion and thinning. The replacement of elastic tissue with a fibroid or scar formation does not permit the vessel wall to withstand the stress and strain of the column of blood thrown by the heart.

#### CLINICAL PICTURES

The clinical picture of syphilitic aortitis varies with many factors. The condition may be present pathologically without any clinical manifestations whatever. The extent of involvement, the localization of involvement, the association of myocardial and coronary disease, all influence the clinical picture.

Pain is one of the most common and interesting symptoms. It occurs in from 60 to 80 per cent of all cases. It was present in 17 cases (70.8 per cent) in this series.

It is probable that this percentage would be even higher if the history were very accurately taken. Often, and sometimes for years, pain may be the only symptom. Allbutt suggests that the intensity of the pain has a direct relationship to the depth of involvement into the arterial wall. The painful sensation may be variously described by the patient. It may be termed knife-like, dull, aching, sore, or merely painful in the sense of constriction, oppression, choking, gripping, or pressing. These painful sensations may be constant,

irregular, intermittent, or may show a periodicity similar to that in gastric ulcer. There is a tendency for the attacks to increase in constancy and severity with the progress of the disease. It is very difficult sometimes to differentiate the pains of aortitis from the pains of an atypical angina pectoris.

The location of the pain or other distressing sensation is as variable as its nature. This very uncertainty and variableness has a certain diagnostic value. Most often it is beneath the sternum. It may be felt, however, over the entire chest, down one or both arms, in the fingers, neck, head, back, epigastrium, and the thighs. There may be considerable opportunity for mistaken impressions when the painful sensation is unusually located, as in the shoulder or epigastrium.

In some cases, the painful sensations may be experienced only on palpation of the body wall. The patient may come to the physician because he has noticed that the pressure of the hand, clothes, or corset is unpleasant. Sometimes deep pressure only will elicit the tenderness, while again, stroking the skin with a piece of cotton wound about a stick may be unpleasant.

Much has been written concerning the mechanism or origin of precordial pain. Early impressions that coronary involvement was essential to the production of pain are passing. Tension and spasm in the heart and aorta seem more probable. Nerves of sensation have not been definitely demonstrated in the heart muscle. It is well known, however, that pain can be produced over a viscus by the mechanism described by Sherrington and Head, even in the absence of demonstrably inherent sensory nerves. The irritation of plaques in the aorta may excite the corresponding visceral segment of the spinal cord, from which centrifugal impulses may be sent to the skin and muscles to be indicated as pain. (Neuhof.) The variable site of the lesions in aortitis can well explain the variable location of the superficial pain or tenderness.

The root of the aorta is enclosed in rich plexus of ganglia and nerves. These and the similar plexus around the heart are derived from the vagus and sympathetic. There is a further nerve supply in the heart from the ganglia and nerve fibers in the auricular bundles and cardiac musculature.

Dyspnea ranks with pain as a frequent and important symptom. It was present in this series in 15, or 62.5 per cent. Dyspnea and

pain are most often associated. Dyspnea is often a very early symptom in aortitis, and its presence in syphilis should never be lightly regarded. The respiratory distress will increase as the pathologic condition advances from aortitis to aortic insufficiency, and then to myocardial insufficiency. Exercise increases the distress. There is another type of dyspnea described by Osler as pulmonary angina. It is also known as paroxysmal dyspnea, cardiac asthma, or air hunger. It is fully described in Longcope's article. These attacks are sometimes classified with angina pectoris, but without pain. They usually occur in advanced cases which have gone on to scar formation, and the development of aortic insufficiency. The dyspnea approaches the type seen in bronchial asthma with prolonged expiration of low pitch.

Other symptoms which may be present are palpitation, tachycardia, hoarseness, arrhythmia, general weakness, fever, and gastric disorders. The grouping of symptoms varies a great deal with the lesion and its extent. Any combination of the above symptoms may doubtless be present in a given case of cardiovascular syphilis, such as aortitis, dilatation, aortic insufficiency, or aneurysm. Irregularity of the pulse is not so common in aortitis as in myocardial disease. This is also true of tachycardia. In the presence of aneurysm, pain dominates the clinical picture.

Fever is not a rare or unusual finding in aortitis. It is not possible to state definitely that the aortitis is the sole cause of the fever on account of the possibility of syphilitic involvement elsewhere; for example, in the liver or other abdominal viscera. It is hard also to exclude coincidental infections in the throat, bronchi, lungs, joints, and sometimes endocardial vegetations in the heart itself. Syphilitic fever runs a low grade course, is irregular in type, and responds readily to specific treatment. It should not be forgotten that coincidental fever from other causes may disappear spontaneously during the course of specific treatment. To be termed specific, a fever should have been under observation sufficiently long to exclude other causes and to afford a control after treatment.

#### PHYSICAL SIGNS

Diagnoses can rarely be made in cardiovascular syphilis from the symptoms alone. Typical attacks of angina pectoris and well-developed aneurysms are exceptions to this rule, and may present a char-

acteristic symptomatology. Physical signs and x-ray findings may be entirely absent in the early stages, but some evidence of trouble may nearly always be determined at the time the patient comes for medical attention.

Inspection may show increased pulsation in the carotids and in the episternal notch. The peripheral arteries may not be visibly sclerosed. The large vessels given off from the arch of the aorta may be raised and strongly pulsating. Abnormal pulsations or indeed heaving may be determined by closely watching the anterior chest wall on either side of the sternum, more often the right, about the level of the second interspace.

Palpation may determine an episternal pulsation. This is suggestive, but not diagnostic of aortic dilatation. This aortic pulsation may be palpated sometimes in emaciated individuals, in patients with hyperthyroidism with atonic vessels, in cardiac hypertrophy with arterial hypertension, and in conditions in which the diaphragm is raised. A thrill may be felt on either side of the sternum.

Increased dullness may be determined on percussion. It is very difficult to determine this early, because of the relations of the first part of the aorta with the superior vena cava and the pulmonary artery.

Auscultation may show changes in the heart tones and the presence of adventitious sounds. Much has been written of the changed tones of the second aortic sound. It is described as clanging, bell-like, sharp, ringing, and by Potain, as the bruit de tabourka (an African drum, quoted from Allbutt). The first heart sound is often rough or impure. The systolic murmur of aortitis may be at first so faint that great care is necessary in examination. It may be heard for long periods of time before the diastolic murmur of valvular involvement is added. The location of the systolic murmur is variable. It may be over the aortic area, or at a distance from this area, as to the left of the sternum in the third, fourth, or even the fifth interspace. More rarely it is heard lower down on the right side of the sternum, or at the ensiform. It may be heard only in certain positions as the left lateral or when the patient bends forward.

There may be heard on auscultation a dry pericardial rub over the aortic area, due to an associated pericarditis. When an aortitis has gone on to dilatation or aneurysm formation, pressure on the



Fig. 1. Male, age 56, farmer, aortitis with aneurysm. Chief complaint is a sensation of pressure or weight in the throat on lying down, relieved by turning on either side. Has complained of symptoms for eight months. Very dyspnoeic. Has pain in chest, but most marked in the right shoulder. Has typical brassy cough. The right pulse is obliterated. Wassermann toun plus positive. Blood pressure, 158 systolic, 92 diastolic.

The x ray shows increased length and tortuosity of aorta. There is an aneurysmal dilatation of the aortic arch involving the great vessels. Note glandular mass to the left of the sternum and just above the aortic knob. The heart is not hypertrophied.



Fig. 2. Male, age 60, aortitis. Admitted here 25 years ago. Chief complaint is dyspnea on exertion. Also has severe pains over the precordium coming on in periods and then disappearing for long intervals. Blood pressure averages 180 systolic, 100 diastolic. Wassermann toun plus positive.

The x ray shows a considerable bulging to the left of the sternum, which is due to an increase in the length of the aorta, as well as the dilatation. The great vessels are dilated. The heart shows moderate hypertrophy.



respiratory passages may produce a peculiar whistling respiration which is increased on exertion.

Attention may be drawn to an aortitis without symptoms by inequalities in the pulses. A water-hammer or collapsing pulse is not rare. This may occur in the absence of aortic insufficiency. The presence of a capillary pulse is unusual in the absence of valvular involvement.

The blood pressure is usually not increased. This fact has some diagnostic value. The pressure of auscultatory signs at the aortic area, such as sharp ringing second tone, a roughened first aortic tone, a systolic aortic murmur with increased blood pressure, are suggestive of aortic atheroma, and not a syphilitic aortitis. The presence of renal complications may increase the tension of the blood in specific cases.

Babinski states that the slowing of the heart, which is a normal reflex response to pressure on the eyeballs, is absent in syphilitic aortitis.

The blood picture has been referred to by Korczynski. In his series of heart cases due to syphilis the blood picture was modified in nearly every case. The small lymphocytes were abnormally numerous. He thinks that this lymphocytic increase suggests the syphilitic nature of the trouble.

#### X-RAY

The x-ray is the most important method of determining dilatation in aortitis. Physical signs such as auscultatory phenomena may appear long before dilatation or other x-ray evidence is obtainable. On the other hand, slight degrees of dilatation may be determined with the x-ray long before other physical signs appear. The aorta may show changes in size or shape. The size and position of the heart influence the shadow of the aorta.

There is considerable variation in the shadow of the normal aortic shadow. The distinction between an unusual normal shadow and a beginning aortic dilatation may present considerable difficulty. The aorta ascendens takes its origin from the base of the left ventricle behind the left margin of the sternum opposite the lower border of the third costal cartilage. From this it passes upwards and to the right to become the aortic arch. This portion of the aorta lies well behind the sternum and well within the shadow of the right auricular

curve. The aortic arch begins behind the right border of the sternum at the level of the upper border of the second costal cartilage. The aortic arch bends upwards and to the left, then turns suddenly backwards to gain the left side of the lower border of the body of the fourth dorsal vertebra. The point where the aorta turns sharply backwards and to the left is variable in the degree of its angle, and also in the precise location of the turn. This point appears as a knob above and distinct from the heart shadow. It appears on the left side of the sternum. The knob increases in intensity as life progresses. It may be absent or ill-defined in early life, but in later life may become so prominent that its precise interpretation becomes exceedingly difficult. Narrow chested individuals with enteroptotic abdomens often show no protrusion of this knob to the left of the sternum. Advanced arteriosclerosis makes this knob appear more prominent by reason of its sharper outline, but does not make the projection actually larger in the absence of dilatation.

In the presence of aortic disease, the intensity of the aortic shadow should be carefully noted. It is doubtful, however, whether the thickening of the aorta or the deposit of lime salts within the tissue of the aortic wall is ever sufficient to permit an x-ray diagnosis in the absence of dilatation. This sign has been emphasized by some writers, but much caution is necessary in drawing conclusions.

The earliest x-ray evidence should be looked for at the point where pathologic lesions are most common, that is, just above the semilunar valves in the suprasigmoid part of the aorta. This part of the aorta should be watched closely for any abnormal pulsation. Inasmuch as it lies behind the sternum, and is covered by the pericardium, pulsation can not often be determined as a diagnostic sign. When the dilatation has reached a sufficient degree, the right border of the ascending aorta can be seen to the right of the sternum. This bulging usually shows with regular borders, but irregularities may appear.

A change in the aortic knob usually appears as a secondary condition, when the dilatation has spread to the arch. It may, however, show a change in the absence of any alteration in the shadow at the root of the aorta. The knob may be more prominent, broadened, or lost. Diffuse dilatation of the aorta is a not unusual finding. This condition may be present in the entire absence of syphilis. It occurs in nonspecific aortitis, atheroma, and in arterial hypertonus.





FIG. 3. Male, age 50, aortitis. Chief complaint was hoarseness and a sense of irritation in the throat. Moderate dyspnea. Wassermann four plus positive, although all history of syphilis is entirely lacking. Entire symptomatic relief following treatment with salvarsan and mercury. Blood pressure, 170 systolic, 110 diastolic. The plate shows an aortitis with dilatation. The heart is not hypertrophied.

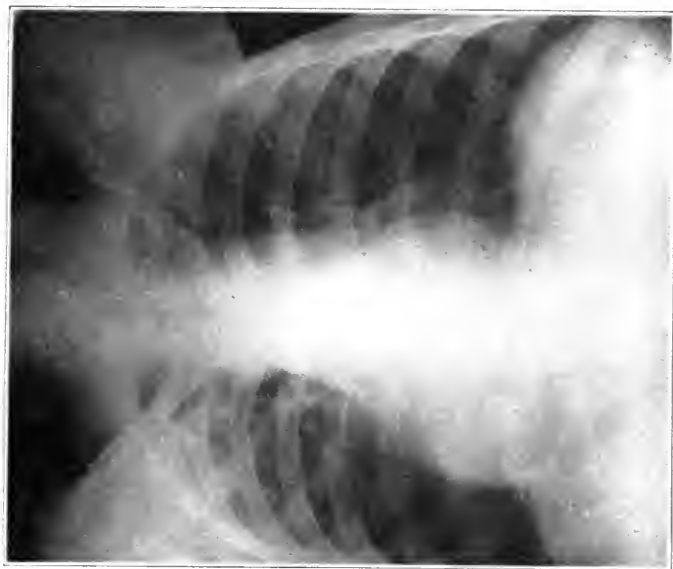


FIG. 4. Male, age 27, clerk. Nonsyphilitic aortitis. Rheumatic fever within the past two years. There is an entire absence of symptoms referable to the cardiovascular system. Blood pressure, 128 systolic, 46 diastolic. Wassermann negative. Physical signs of aortic insufficiency. The x-ray shows moderate dilatation of the aorta. The heart is much hypertrophied. The great vessels of the neck are dilated.



This diffuse dilatation produces an increase in the transverse diameter of the aortic shadow. Beginning at the base of the aorta, the right border projects beyond the border of the right auricle. The aortic shadow is also raised. The aortic knob along the left sternal border may lose its acute angle, and become less prominent, flat, or broadened. As the process advances, the length of the aorta may increase with an increase in the height of the upper border of the aortic arch.

Changes in the heart shadow is an important part in the interpretation of an aortitis. The heart shadow may be variable from normal reasons, from valve lesions, aortitis, or arterial hypertonus. An important differential point between specific and nonspecific aortitis is to be looked for in the increased shadow of an hypertrophied left ventricle. Such an hypertrophy when marked in a doubtful case speaks in favor of a nonspecific process. Hypertrophy of the heart may occur in the absence of aortic valvular insufficiency.

#### COURSE OF THE DISEASE

Comparison of the number of cases of syphilitic aortitis found at autopsy and the number determined clinically makes it clear that many cases run a latent course. This is true even with the concession that some of the cases are overlooked and not diagnosed. A study of the reported cases shows that this period of latency does not depend altogether on the treatment instituted. Many of the latent cases have been poorly treated, and some not at all. It is true, however, that cases which progress from simple aortitis to dilatation, aneurysm, aortic insufficiency, and myocardial disease are much more apt to be the insufficiently treated ones. Patients whose vascular conditions tend to progress are peculiarly resistant to treatment. The appearance of signs of an aortic valvulitis while the patient is under treatment is of grave portent. Sudden death is always to be considered as a possibility.

The course of the disease may run in periods of greater activity. As long as the evidences of the disease process are from signs only, the course of the disease may be comparatively favorable. When, however, to these physical signs are added symptoms, the condition becomes at once more serious. Symmers states that death ensues in from two to three years after the appearance of symptoms. This

period is often greatly lengthened. Involvement of the coronary arteries and the aortic valve renders the disease picture much more serious.

#### NONSPECIFIC AORTITIS

Much confusion may rise from the fact that a nonspecific aortitis may exist in a syphilitic patient. Such types of aortitis may occur following rheumatic fever, smallpox, typhoid fever, influenza, and other infections. The aortic lesions following rheumatic fever are more common, and may be considered as the type of nonspecific aortitis. Rheumatic aortitis and aortic insufficiency are accompanied almost invariably by mitral disease. Pain is a more constant accompaniment of specific aortitis than in the nonspecific form. Rheumatic aortitis manifests a greater tendency to spontaneous subsidence than the specific form. When aortic leakage has been brought on, with or without coronary involvement, the syphilitic cases run a graver course.

Attention has been drawn by Grau and Stadler, Allbutt, and others to the fact that in syphilitic aortitis, there is a relative absence of left ventricular hypertrophy. There may be hypertrophy, but it is less marked and less stable than in nonspecific forms. Grau goes so far as to state that if compensation is good in aortitis with aortic insufficiency, the disease process is not due to syphilis. It has been pointed out by Allbutt that this lessened likelihood of a stable ventricular hypertrophy in syphilis may be due to a greater degree of coronary involvement. He believes that blockage of the coronaries due to syphilis will be associated with a far greater degree of myocarditis than in blockage of the coronaries due to arteriosclerosis. In nonspecific aortic insufficiency the heart may gradually strengthen and the hypertrophied left ventricle be sufficient to maintain good compensation for many years. Another reason is the fact that the myocardium in syphilis is invaded with spirochetes from the beginning of the disease and, therefore, contains a permanent source of weakness.

#### AORTITIS AND CORONARY INVOLVEMENT

The question of aortitis can not be discussed without some consideration of coronary involvement and angina pectoris. The status of the relationship between coronary disease and angina pectoris

is not at all settled. Allbutt has long emphasized the role of aortitis in the production of anginal pains. The location of the coronary orifice is such that involvement of them readily comes about in the progress of an aortitis. The orifices lie well below the point of usual aortic involvement in the beginning and are attacked in the downward extension towards the aortic valves. The coronary orifices may, however, be involved in a pathologic process of small extent. A small hyaline plaque may be so located that partial or complete obstruction of the coronary does not extend far along the course of the vessels, regardless of the severity of the aortic process itself.

Bouchard states that in 261 consecutive cases of syphilis, 12, or 4.6 per cent, had angina pectoris. It is not at all possible to infer the presence of coronary disease in cases of angina pectoris. It may happen that an adhesive pericarditis at the base of the heart may so constrict the coronaries or aorta that angina may result without actual disease of the coronaries at all. Brooks calls attention to the fact that the state of the peripheral arteries is no criterion by which to judge the condition of the coronary arteries. The latter may be involved to an advanced degree with soft and apparently normal peripheral vessels. If the coronary arteries have closed very gradually, the effect on the myocardium may not be at once apparent. Sudden closure is fatal.

#### DIAGNOSIS OF AORTITIS

The diagnosis of an aortitis has to do with its etiology, as well as its presence. More attention is now being paid to the presence of nonspecific types. It is not at all justifiable to assume all cases to be syphilitic. The two types may be associated. An aortitis may appear in a syphilitic without any other physical sign of syphilis. The Wassermann is of great value, and if positive, proves that a patient has syphilis, but not that the lesion under consideration is due to syphilis.

A syphilitic aortitis should be kept in mind in the presence of chest pains, dyspnea, and a positive Wassermann. If the individual is under middle age, the probability of syphilis is greater. Dullness from an aortic dilatation of an aneurysm means an advanced state, at which time the ease of diagnosis is much greater. The presence of aortic signs, a negative Wassermann, and the absence of a syphilitic

history, should lead to a very searching investigation of the entire body for evidence of lues. There may be bony changes, scars, or areas of pigmentation in the skin, atrophy of the base of the tongue, or fixed and irregular pupils.

The therapeutic test is very valuable in a diagnostic way and is justified if all other means of diagnosis are wanting. It will not often be found necessary.

#### AORTITIS AND TABES

The association of aortitis and tabes is of great interest and has diagnostic value. Stadler found aortic disease almost the rule in tabes. The tabetic signs usually precede the aortic, and the presence of the former should suggest the possibility of aortic disease. This time relationship is probably only an apparent one due to the fact that the stage of latency may persist longer in the aorta without symptoms.

#### PROGNOSIS

The prognosis is dependent on the time of diagnosis. Early recognition often enables the treatment to stop the disease process before it has gone on to irreparable damage. The location of the lesions directly influences the prognosis. Disease of the suprasigmoid portion of the aorta, often involving the coronaries and aortic valves, is always serious. The frequency of myocardial disease in conjunction with aortitis is a matter of grave moment. The duration of life after the diagnosis is made is very variable. Different reports give from two to five years. Many cases, especially with severe myocardial involvement or angina pectoris, may die suddenly. It is not unusual for such patients to live many years, but they are exceptional. It is entirely probable that with the more intensive treatment of the present time, the duration of life will show a decided increase in statistical studies.

#### TREATMENT

Many cases of aortitis become latent or are arrested without involvement of the valves or coronaries and with undue dilatation. It remains for future study to show whether the intensive treatment, so much advocated at the present time, will lessen the incidence of

cardiovascular syphilis. The knowledge that involvement of the nervous system and the cardiovascular system takes place very early in the course of syphilitic infections should place a serious responsibility on the physician who first treats the patient.

It may be said in a general way that syphilitic affections of the heart itself, and also the mediastinum respond better to treatment than affections of the aorta. No type of treatment should be expected to remedy mechanical defects. Symptomatically much may be expected in certain cases of aortitis. The alleviation of symptoms, such as pain and distress in breathing, is often very striking. This alleviation may take place without demonstrable changes in the physical signs or the x-ray findings.

Potassium iodide has been used in treatment since the days of the earliest recognition of cardiovascular syphilis. It does not appear that beneficial results are attained, although favorable reports are not lacking in the literature.

Mercury should be used intensively. The frequent association of kidney involvement with chronic cardiovascular disease should lead to a cautious watch of the urine. There are comparatively few cases, however, in which the irritant action of mercury on the kidneys will compel the drug to be stopped.

Salvarsan has been used in many series of reported cases. It does not appear that the early warning against salvarsan in cardiovascular syphilis has been entirely justified, but subsequent experience has shown that there was ground for Ehrlich's caution. It has been suggested by Longcope that the temporary increase of symptoms which may follow an injection of salvarsan may represent an Herxheimer reaction, and that the increased tissue reaction toward the toxin liberated by the destroyed spirochetes is at fault. This tissue reaction is most dangerous in cases of angina pectoris, both in reality and theoretically. Some of the most alarming reactions follow in the case of angina pectoris. This is to be explained by the hypothesis that the tissue reaction from the liberated toxins causes a closure of the coronary orifices in greater or less degree. This possibility should lead to the use of smaller doses than the maximum.

The actual results of treatment are difficult to judge. It may be said in a general way that specific treatment should not be expected

to change the anatomic conditions. The most marked results appear in the relief of symptoms such as dyspnea and pain. An improvement of the general condition of the patient may be noted sometimes. There is a tendency to recurrence of the symptoms after relief by salvarsan. This tendency is so marked that it may be expected almost, even after the most thorough course of treatment. If the patient can be kept under observation, it is best to keep up the treatment at intervals for long periods of time. If the patient has an interval of freedom from his pain and dyspnea after one or more injections of salvarsan, he should be requested to report for further treatment whenever his distress recurs or becomes more marked. It may be possible in this way to carry the patient along for many years without undue discomfort.

Increasing experience leads to the conclusion that when cardiac symptoms due to an aortitis and its allied conditions have once appeared, a so-called cure should not be expected. The word *cure* is used in the sense of permanent relief of symptoms. The realization of this fact should lead to a sense of increased responsibility in treating these cases. It means that the physician is putting off an inevitable end by means of his skill.

#### SUMMARY

Syphilitic disease of the aorta is a much more common affection from the pathologic point of view than from the clinical. Autopsy studies show a much greater incidence of aortitis than clinical findings. The disparity between these findings should lead to an endeavor to bring the clinical findings to a point more closely approximating the pathologic percentage.

Syphilitic aortitis should be specifically looked for in every patient who has had syphilis without waiting for symptoms and signs to become prominent. Syphilitic aortitis is present in from 5 to 10 per cent of all patients having syphilis. It is more common between the ages of 30 and 50.

The length of time which intervenes between the beginning of infection and the first appearance of symptoms is very variable; it may be but a few months after the initial infection, or the period may be delayed for twenty or more years.

The most important symptoms are pain, dyspnea, palpitation, hoarseness, fever, and gastric disorders.



The physical findings show variable pictures, depending on the location of the lesion, the extent of involvement, and the implication of the large arteries given off from the aortic arch.

The x-ray is the most important method of determining the dilatation of the aorta. Physical signs can almost always be determined before the appearance of dilatation.

The course of the disease is variable, and may run a prolonged period of inactivity or latency. When symptoms appear, the condition becomes at once more serious.

The average duration of life after symptoms appear is from three to five years.

The treatment of aortitis is the treatment of syphilis. It is probable that the intensive treatment of the present day will lessen the evidences of aortitis. Great relief may be expected in a systematic way following treatment, but changes in the physical signs or anatomic conditions very rarely occur.

Caution should be used in giving large doses of salvarsan in the presence of aortitis, on account of the appearance of severe reactions.

## CONDYLOMA OF THE UMBILICUS

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SYPHILIS of the umbilicus is an extremely rare affection. The great master, Fournier, in a personal observation of one hundred ten extragenital chancreoids and ten thousand chancres, found only sixteen of the abdomen. Rille, in 1912, collected from the literature eight cases of primary syphilis, and in 1914 added a further contribution to the subject and referred to these additional cases. Blum, in 1876, in his article on tumors of the umbilicus in the adult, mentions a case of a man, age 36, whom he thought had syphilis of the umbilicus. According to Cullen, from the clinical picture the case could easily have been one of umbilical concretion.

The case of Fischer, reported to Cullen, is perhaps the most authentic convincing case of primary syphilis of the umbilicus yet reported. There have been a number of ulcerations observed in the umbilicus of infants, at or shortly after birth, which have been considered syphilitic, notably the cases reported by Bertherand and Merklen, and Huntinel. The umbilical ulcerations described by these authors were usually associated with certain characteristic symptoms of hereditary lues; e. g., coryza, anal fissure, bone changes, and erythema of the buttocks.

From a review of these cases, Cullen is of the opinion that, if not in all, at least in the majority, the diagnosis of syphilis is doubtful. The umbilical pictures presented by them are similar to those due to the umbilical infections which were so commonly seen formerly, shortly after birth. Anatomically they show no difference, and even histologically Cullen maintains that the pictures of these supposedly syphilitic lesions of the umbilicus are by no means conclusive. At the present time, all doubt concerning the syphilitic nature of these umbilical ulcers could at once be removed by the examination for spirochete pallida.

The case of condyloma of the umbilicus which I desire to report

is perhaps unique. Cullen, in his classical and exhaustive monograph "The Umbilicus and its Diseases" does not mention a case. Those of us who know Cullen's Herculean labors on this subject and his pride in making his volume the storehouse of all things umbilical, feel that only because condyloma of the umbilicus is unique, is the lesion not mentioned. For the same reason, it would be folly and unnecessary repetition to review the literature to learn of the possible presence of this rare condition. I have borrowed liberally from the work of Cullen in the preparation of this paper.

A brief history of the case of condyloma of the umbilicus observed is as follows:

#### CASE HISTORY

Nov. 16th, 1916.—F. F., referred by Dr. E. L. Pessagno, white, male, steel-worker, complains of sores around anus. He has been in good health all his life. No previous venereal diseases except a sore on penis eight weeks ago, the incubation period of which was nine days. The sore healed in a month under local treatment.

*Present Condition.*—About five weeks ago a patient noticed a severe itching around the anus: this was followed in several days by the appearance of a number of sores which gradually became larger and more painful. During the past two weeks a warty mass has appeared around the anus: this is so painful and uncomfortable that the patient has no rest. During the past day or two patient has had a burning and itching sensation in the umbilical region: this he attributes to an elastic belt which he wore, and which rose to the level of his navel. He also complains of a sore throat, and a sore on the inside of lower lip.

Examination reveals the external genitals normal, except for the presence of a small elevation on the right lip of meatus and an indurated area on the left side of the penis near the frenum. Both these places are the remains of the original sites of infection, which were evidently two in number. No examination of these for spirochete pallida had been made before they healed. The inguinal glands of both sides are enlarged and painless. Surrounding the anus there is a ring of condylomata, which, on microscopic examination, shows many spirochete pallida. A faint macular rash can be seen over the body. The right tonsil is covered by a mucous patch and a patch is seen on the inner side of lower lip. A cervical adenitis is present also.

Inspection of the umbilicus shows a slightly reddened area around it. On everting the umbilicus, three distinct and typical condylomata are seen. Microscope examination of these shows many spirochete pallida present.

*Treatment.*—Patient was given four intravenous injections of salvarsan of 0.3 gram each, at weekly intervals. On December 4 there was slight itching around the anus, but the pain had disappeared. Condylomata of the umbilicus were drying up. On December 12 the condylomata of anus were almost dried

up and no longer caused discomfort. The condylomata of umbilicus were dry and smaller. At date of writing the lesions have all cleared up.

#### DISCUSSION OF CASE

The most interesting feature of the case is the wearing of the belt around the umbilicus, whose irritant action was undoubtedly the predisposing factor in the production of the lesion. The diagnosis of the lesion was easily made by its typicalness, being exactly similar to the condylomata ani, which the patient also had. The certainty of its luetic nature was demonstrated by the presence of the spirochete pallida, and its rapid disappearance after the institution of antisyphilitic treatment. Dr. Cullen was kind enough to observe the patient and concur in the diagnosis.

## MASSES IN THE NECK

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ONE of my professors of surgery was in the habit of impressing on his students the necessity of making a diagnosis of the most common disease if one wanted to be right in the majority of instances (Dr. Edmond Souchon). This is a good procedure, but in the case of masses in the neck, it will lead to error, if at the same time one does not keep in mind the many possible sources of error. I have been impressed by my own difficulties and the apparent difficulty which some of my colleagues have had in making a correct diagnosis in instances of large masses in the neck, hence this report. In more than 16,000 cases at the Touro Infirmary Surgical Clinic, about 125 cases of cervical conditions have come under observation. Of this number some have been tuberculosis, syphilis, lymphosarcoma, medullary carcinoma, Hodgkin's disease, metastatic carcinomata, retropharyngeal abscesses, burrowing through the connective tissue planes, branchial cysts, thyroglossal cysts and carotid body tumors.

Some of these cases have presented so many interesting and puzzling features, that I have thought it worth while to collect them and to present them in this form, if no other benefit than the ocular demonstration of the pictures of these cases is derived, the paper will have served its purpose. To me they have served the purpose of impressing the difficulties of diagnosis, and the importance of excluding all of the possibilities before doing anything. In order to exclude the possible causes one must first consider the age of the patient, the time of onset, the duration of the "growth" and the source of infection. To do this certainly the lymphatic drainage to the area involved should be thoroughly understood. The various blood examinations must be tried, as well as a section of tissue examined. This last named procedure will alter many a "positive diagnosis" which has been made clinically.

A consideration of neck "growths" and infections would be in-

complete without the inclusion of that interesting, yet infrequent, group of cases which come under the head of congenital cysts and fistulæ of the neck. Since they are the easiest to diagnose, when proper consideration is given to the duration of the "growths" and because the subject is so slightly touched upon even in our larger "systems," we will consider them first. In Keen's Surgery all that we will find on the subject is: "Congenital sacs of the branchial clefts are to be classed with the fistulæ and require the same treatment." McKenty studied 30 cases of tumors of the neck of congenital origin. He observed: "Tumors of interest from an embryologic point of view occurring in the neck are of great importance on account of their difficulty of diagnosis and their comparative frequency." A point of great importance is noted also by McKenty; "these tumors are frequently diagnosed as tubercular glands." The following two cases, the histories and photographs of which are given below are included because the true diagnosis could easily have been overlooked, *if the history of the tumor having been noted soon after birth by the parents or nurse had not been taken into consideration.*

#### BRANCHIAL CYST

CASE A. L., 9693. Age 5 years; colored female, April 23, 1913.

*Diagnosis.*—Branchial cyst.

Mother noticed a swelling behind the ear when the child was five months old. The mass has gradually increased in size.

*Examination.*—There is a mass about two inches in diameter, noticed on the left side of the neck, the upper limit of which extends to the mastoid process, downward to about the level of the hyoid bone, it occupies the position of the upper portion of the sternomastoid muscle. The mass is movable under the skin and seems to have deep attachments, it is nodular, and seems to be cystic.

*Operation.*—Under ether anesthesia, she was operated at the Illinois Central Hospital. The cyst was excised as seen in the Fig. 3. The mass did not recur, she had no further trouble. The contents of the mass was a gelatinous material. (Figs. 1, 2 and 3.)

CASE E. B. December, 1914.

*Diagnosis.*—Branchial cyst.

Examination showed a small movable mass on the right side just about the level of the thyroid cartilage. Mass has been noted since early childhood. Advised operation: Child did not return. (Fig. 4.)

Since many of the cases came in childhood, and since the location of the cyst, due to the persistence of part of the second cleft, is near



Fig. 1.—Branchial cyst.



Fig. 2.—Branchial cyst.



Fig. 3.—Same as Fig. 2 after operation.





the angle of the jaw, one must carefully differentiate these tumors from tuberculous glands. The branchial cysts are circumscribed, movable under the skin, and impart the sensation of fluid content under tension. *Transillumination will aid in diagnosis.*

The correct diagnosis of these congenital cysts is essential pre-operative, because the operator should be prepared to encounter difficulties in removal due to the intimate relationship existing between the ramifications of the cyst walls and the deep structures of the neck.

Incomplete removal may result in a fistula opening internally on the pharyngeal wall, and externally on the surface. Branchial cysts which are due to persistence of third and fourth cleft remnants must be differentiated from carotid body tumors, tuberculous glands, and metastatic growths.

#### CAROTID BODY TUMORS

*Carotid Body Tumors are Rare in the Young.*—The carotid body from which the tumors arise has been studied carefully by Keen and Funke, Winslow, Callison and McKenty, and many others. (Bibliography can be found in Callison and McKenty's article.\*)

Divergent opinions have been expressed as to the origin of these tumors. Winslow states: "The carotid body is not a gland in the usual acceptance of the term, but appears to belong to the sympathetic nervous system and to the chromaffin group."

Callison and McKenty describe it as: "A body 5 mm. long, 3 mm. wide, and 2.5 mm. thick, lying in the bifurcation of the common carotid artery of *doubtful* embryologic derivation, of undetermined function, inconstantly present, but occasionally giving rise to tumors of definite structure, that is the substance of our knowledge of this gland, so-called. The nerve supply to the carotid body is abundant; it receives branches from the vagus, glossopharyngeal, and the superior cervical sympathetic: fibers pass from the vagus, glossopharyngeal and sympathetic and form a plexus just in front of the carotid body."

In spite of the fact that recently a great American surgeon has said "these curious little tumors have been dissected, studied, and described almost as *nauseam et ad infinitum*," we find in a paper by Winslow, before the American Surgical Association in 1916, the

\*Ann. Surg., 1913, lviii.

following significant statement: "The occurrence of tumors of the carotid ganglion is of sufficient infrequency not only to justify, but to make desirable the recording of all such cases." It is also significant to note that of 54 cases studied by Callison and McKenty, only seven cases were recognized before operation. Thus it would seem that it is important that a more widely disseminated knowledge of the symptomatology and pathology is desirable.

Reviewing the literature we find that the age of the patient presenting himself for operation, varies from 7 to 70, the majority occurring above the age of 20. The duration of the growth before operation varies from a few weeks to twenty years. The greater number of cases have had a slow growing painless mass for many years. Because of the absence of pain and other subjective phenomena, the patient waits.

In a number of reported cases the patient has complained of aphonia, dysphagia, dyspnea, hoarseness, and cough, and in one case a mild exophthalmos was noted. When the nerve supply to the carotid body and the proximity of the plexus referred to above are considered, it is not difficult to understand the presence of the subjective phenomena just mentioned. These are important and should aid in making the differential diagnosis more often prior to operation.

Carotid body tumors are elliptical; they vary in size, extending "upward to the base of the skull or downward to the clavicle in some cases. They are usually firm, smooth, movable laterally, but not vertically." The growth is encapsulated, and does not infiltrate the surrounding tissues unless its malignancy is advanced." (Winslow.)

One case of carotid body tumor has been observed in this series. The diagnosis was made preoperative. The clinical history of the case is as follows:

CASE A. E. Age 55 years, July 26, 1917.

*Diagnosis.*—Carotid body tumor (Fig. 5).

*Complaint.*—Mass in right side of neck which interferes with eating. Insomnia, because of coughing. Operated last year. The doctor was called after he had made an incision. He did not proceed with the operation. The mass has recently increased in size.

*Examination.*—There is a mass on the right side of the neck, which extends from the tip of the mastoid, down to the level of the thyroid cartilage, four and one-half inches in diameter. The mass is soft, movable, but not fluctuant, not pulsating. Over the surface of the mass there are several small nodular masses prob-



Fig. 4.—Branchial cyst.

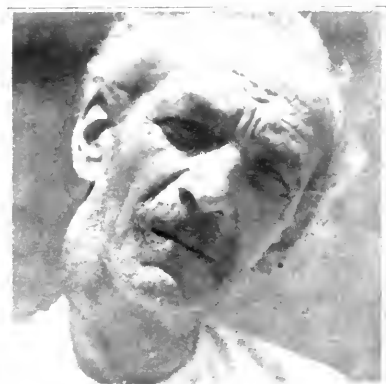


Fig. 5.—Tumor of carotid paraganglion or glands.



Fig. 6.—Metastatic carcinoma of neck.



Fig. 8.—Lymphoblastoma.



Fig. 7.—Primary growth on tonsil. Metastatic carcinoma. Lymph glands.



ably lymphatics. Tonsils: Negative, except that the right is pushed forward by the mass; the tongue and buccal mucosa are negative. He has no similar masses anywhere else on the body.

Venereal history is negative. Phenolsulphonphthalein test—36% two hours.

*Operation.*—Believing the mass to be either a carotid body tumor or a lymphosarcoma, I operated July 30, under ether anesthesia. An incision was made from the tip of the mastoid along the anterior border of the sternomastoid as far down as one inch above the sterno clavicular joint. After incising and retracting the platysma, several large veins came into view. The sternomastoid had been displaced outward by the prominent mass. A search was made for the carotid below and above the level of the omohyoid. This muscle had evidently been cut at the previous operation.

A large thick walled nonpulsating cordlike structure occupied the anatomic position of the carotid. This "cord" entered the growth.

It was impossible to remove the mass without cutting the "cord." Below the level of this cord the innominate and subclavian could be felt. The internal jugular vein was closely adherent to the tumor. In order to avoid serious hemorrhage, a large segment of the internal jugular had to be removed. The mass was then removed. On section it was found to contain a *vessel* with a clot in its lumen.

After the operation was over the patient had a respiratory failure, which was succeeded soon by cardiac failure. After five minutes' artificial respiration the patient began voluntary respiration. Amyl nitrate, atropine, and oxygen were administered and the head of the table was lowered. He never regained consciousness, pupils never again reacted to light. Patient, however, became restless during the afternoon. He moved both extremities. Temperature rose to 105.8° before death, which occurred at 6:30 July 30, 1917. No autopsy.

This case, as all similar cases, presented the necessity for differentiation from primary lymphosarcoma, metastatic carcinoma of the lymph glands, aneurysm, gumma, tuberculous cervical adenitis, and aberrant thyroid. The points of differential diagnosis can best be presented as cases of each type are discussed.

Before taking that phase up it may be well to mention Callison and McKenty's statistics of 60 cases:

Fifty-four cases came to operation; 22 died soon after operation. In 21 cases there were complications, 4 had hemiplegia. "(All three carotids were ligated in 32 cases.)" In 4 cases the voice was affected; in 5 cases there was deviation of the tongue. In 4 cases the pupils were altered, and in 4 cases there was partial paralysis. *These statistics emphasize the anatomic difficulties to be surmounted if a successful outcome is to result.*

The accompanying photograph of a case of metastatic carcinoma of the lymph glands may have been mistaken as to location and

size for a carotid body tumor; if, however, a primary growth had not been present on the tonsil. Pain was intense and there was a rapid deterioration of the patient's general health. These secondary growths infiltrate the surrounding tissues. (Figs. 6 and 7.)

#### PRIMARY NEOPLASMS IN THE NECK

Coley, in 1916, discussing primary neoplasms of the lymphatics, states: "While in many cases it is possible to make a correct diagnosis from the clinical signs alone, together with the history of the case rapidity of growth and blood examinations, in most cases a positive early diagnosis can not be made without a microscopic examination, and not always then. I do not believe that there is much risk in an exploratory operation for the removal of enough tissue for a microscopic examination."

In this latter opinion Greenough does not concur. In his report before the American Surgical Association in 1917, we find the following: "A block dissection of the area involved, including the adjacent lymph nodes, is recommended in preference to the excision of a single suspected node. Where obviously a hopeless case of cancer is shown to be present, removal of a single node may prevent a useless operation, and is to be recommended."

Coley's studies, based on 167 personally observed cases indicate that the round-celled sarcoma is the most frequent type of growth. *The mass usually begins as a single nodule which infiltrates the surrounding tissue. It increases rapidly in size, is associated with pain, and only infrequently leads to metastases.*

Compare the clinical picture of Hodgkin's disease. We expect enlarged glands, "usually beginning in the cervical region on one side, soon involving the opposite side. The glands are freely movable and more or less discrete or may become fused; they are firm and may remain unattached to the skin. The axilla and groin later become involved. The liver and spleen may be enlarged; the general health of the patient deteriorates and death results." This group of cases offers the greatest difficulty in arriving at a correct diagnosis and are included under the group of so-called primary neoplasms of the neck.

This is not done because of an adherence to the views of anyone

else, but because of personal difficulties as illustrated by the following clinical cases.

CASE J. S. Colored male. (Fig. 8.)

*Clinical Diagnosis.*—Hodgkin's disease.

*Pathologist's Diagnosis.*—Lymphoblastoma.

*History.*—During November, 1915, he noticed a swelling in the right side of his neck. At first there was the feeling of an ordinary stiff neck. The swelling increased rapidly until about Christmas time the mass attained the present size. During February, 1916, he noticed a swelling in the left axilla; April 15, 1916, a mass appeared in the left inguinal region. He feels strong, his appetite is good, and he is able to work every day. The main discomfort which he complains of is "catarrh." (There is a constant discharge from the nose.)

*Examination.*—There is a large mass in the right side of his neck which extends from the tip of the mastoid to the clavicle, from the sternal notch almost to the mastoid process; the mass is nodular, hard, slightly movable. There are no sinuses. No pain on palpation. On the left side of the neck there is a similar smaller mass. In the inguinal region and in both axillæ there are enlarged glandular masses. One of these masses was removed for diagnosis. The report "lymphoblastoma," is more suggestive of sarcoma than Hodgkin's (Lanford), seemed to negative the clinical diagnosis.

CASE W. J. Age 35, colored male, May 22, 1915. (Figs. 10 and 11.)

Two months ago he noticed "lumps on both sides of his neck." There has never been any pain associated with the masses. Three weeks ago his ears began to run a little at night. Sore on penis four years ago.

He has lost ten pounds during the last nine weeks. No night sweats.

*Examination.*—Swelling on both sides of neck, below the ears, more marked on left side, no redness, no pain on pressure. Palpation reveals enlarged glands under both sternomastoid muscles, more pronounced in upper third. Glands are discrete. No palpable enlarged glands elsewhere. Wassermann negative. A small gland was removed under the most careful precaution for the purpose of culture and section.

*Clinical Diagnosis.*—Hodgkin's disease; histologic diagnosis was tuberculosis.

From the histories, clinical diagnosis, and the pathologist's finding, it is seen that the diagnosis of Hodgkin's disease has been made in a lymphoblastoma more suggestive of sarcoma than Hodgkin's (Lanford), in a medullary carcinoma and in tuberculosis. (Fig. 9.)

In making these errors, we are not alone. These border line cases which seem to answer the clinical description of Hodgkin's disease so well continue to give trouble in diagnosis, in spite of the clear description of the disease when it is described independently. The diagnosis of Hodgkin's disease can not be made with certainty without the aid of the histopathologist's report.

Even in this field there is still controversy. Coley (1916) says,

"There is much evidence pointing to a very close relationship between the groups of tumors at present designated as malignant tumors, carcinoma, and sarcoma, and the group regarded as Hodgkin's disease."

On the other hand, Bunting (1914), after studying 28 cases says, "the study of these cases from a pathologic standpoint has strengthened the conviction that the lesion of Hodgkin's disease is essentially of inflammatory nature. Careful search will in the majority of cases reveal a primary inflammatory lesion which was present before the enlargement of the glands occurred. This is most apt to be the tonsils, teeth, or nasal sinuses. Hodgkin's disease is an infectious disease due to a diphtheroid organism, the bacterium *Hodgkin*."

Efforts were made by Dr. John Lanford to isolate the specific organism from glands removed in suspected cases. *He was able to obtain the diphtheroid in cases which were certainly not Hodgkin's disease.* His report in one of our cases suggests his adherence to the neoplasm theory.

Besides the diphtheroid, Bunting has described a blood picture which he considers of diagnostic value, even without a history and at a distance. Bunting divides the blood picture according to the stage of the disease into two groups:

(1) Early stage of the disease, duration one year or less. Normal or slight increase in total leucocyte count, with normal or decreased percentage of polymorphonuclear neutrophils.

(2) Later stage of the disease. Marked leucocytosis, running as high as 100,000. Polymorphonuclear count increased, varies between 72 and 90 per cent.

"One may summarize the blood findings then as follows: Throughout the disease there are two constant features, an increase in blood platelets and an absolute increase in the transitional leucocytes.

"From the foregoing it may seem there are sharply marked blood changes in Hodgkin's disease. The question naturally arises, are they of value in diagnosis of doubtful cases? It is my belief that, given a case of chronic glandular enlargement and without any suppurative process and the blood picture which I have designated as the late or secondary, the diagnosis is established; given the chronic glandular enlargement, and the primary blood picture diag-





Fig. 9.—Medullary carcinoma.



Fig. 10.—Tuberculous cervical adenitis.



Fig. 11.—Tuberculous cervical adenitis.



nosis is somewhat more difficult; but, in my experience can in a great majority of cases be made with certainty." (Bunting.)

The diagnosis usually lies between Hodgkin's disease and tuberculosis. There are apparently two distinct pictures in tuberculosis of the glands, that are found when such a change has occurred. In tuberculosis Bunting found "quite constant low eosinophile count associated with a low transitional count."

I have quoted extensively from Coley and Bunting because early diagnosis is necessary if effective aid is to be given these unfortunates. *Be it neoplasm or of infectious origin, and it seems to be the former, a late diagnosis means a fatal termination irrespective of the treatment. Early diagnosis can only be made by the removal of a gland for examination and the blood examination.*

One of the cases diagnosed Hodgkin's disease proved to be tuberculous. This error in diagnosis was caused by just one of the many unexpected variations of tuberculosis in its invasion of the lymphatics. Because of the general acceptance of teaching, such as the following abstract from our leading surgical work: "Chronic hyperplastic enlargement of the cervical lymph nodes is almost tuberculosis," and further because the clinical picture of syphilitic involvement of the lymphatic of the neck is not generally understood, errors in this direction are constantly being made.

Enlarged glands associated with fever, emaciation and sinus formation are ordinarily considered of tuberculous origin without further ado, and often operations are resorted to which prove eventually to have been unnecessary.

*Fusion of the glands by a periadenitis should not be considered evidence of tuberculosis, to the exclusion of other conditions.* The periadenitis is an indication of a secondary infection and is often present in hyperplasia of lymph glands due to syphilis, Hodgkin's disease, and lymphatic leucemia, as well as tuberculosis. Hence these conditions must be eliminated before the diagnosis of tuberculosis can be accepted. *The size of the gland does not eliminate syphilis.*

CASE A. H. Colored female, age 22 years, Feb. 3, 1917. (Fig. 12.)

*Diagnosis.*—Tubercular cervical adenitis. Bilateral.

About one year ago the left side of her neck began to swell. She was able to feel a large lump below the ear. The mass increased in size and for about five months it remained hard, then she noticed it began to soften, two weeks later she says it "began to run from two places." There would be an alternate

period during which the sinus would open and close. The discharge was greenish and flakey. About four months ago the right side of her neck began to swell in the same manner as the left had, one month later the right side of the neck began discharging. Seven different sinuses have formed in the neck. No pain until one week ago, and then it was noted behind the ear (right). Not married; one full term baby, which died about five minutes after birth. Denies venereal infection, no sore throat; headaches chiefly during the day.

*Examination.*—Patient is stout. The neck is very large, so much so that on the right side there is apparently no line of demarcation between the cheek and the neck. The left side of the neck has its largest masses in the posterior cervical triangle. There are a number of sinuses in both sides of the neck, some are actively discharging now. The glandular masses are discrete in places, but in the larger number of instances they are matted together. They are adherent to the skin and movable with it. There is some dullness in the chest, as far down as the 3rd interspace. She has no discomfort breathing. There are some palpable glandular masses in both axillæ. Epitrochlear glands are barely palpable. Pyorrhea alveolaris.

A single gland was removed to confirm the diagnosis. This contained many areas of caseation. Pathologic report S-16-119. "Tubercular Adenitis." Treatment increasing doses of tuberculin (O. T.) and cod liver oil. She remained under observation until March 28. Improved.

CASE S. B. June 6, 1916.

*Diagnosis.*—Syphilis or tuberculosis. (Figs. 13 and 14.)

Had an abscess on neck in December, 1915. This was "lanced," the wound discharged for one month. About January, 1916, she noticed that the right side of her neck began to swell. The left side also began to swell during the same month. She has lost ten pounds in weight.

*Examination.*—On the left side of her neck extending from below the angle of the jaw to the clavicle there is a large mass of "glands" which are adherent to the skin, they are apparently fused together by a marked amount of periadenitis. In the lower portion of the neck, about one inch above the clavicle there is a transverse scar which has an irregular ulcerating base; the edges of the scar are violaceous; there is some induration. There is very little discharge from the ulcer. On the opposite side of the neck there is a similar, but smaller, mass. The masses are not painful; they are movable with the skin on the underlying soft parts. Temperature 99.8°.

*Wassermann positive.*—Salvarsan, three doses between June 10 and July 8, 1916. The masses have almost entirely disappeared. She has gained in weight. Feels fine. The sinuses in the neck have healed.

These cases illustrate the difficulty in making a clinical diagnosis, if we continue to consider periadenitis, febrile reaction, degenerative changes, and sinus formation evidence of tuberculosis. In one of the cases cited a single gland which was removed cleared up the diag-



Fig. 12.—Tuberculous cervical adenitis.



Fig. 13.—Lymph gland enlargement due to syphilis.



Fig. 14.—Lymph gland enlargement due to syphilis.



nosis, whereas in the other the positive Wassermann and the marked improvement under treatment proved the other to be syphilis.

*Operation should not be decided upon in the adult, without first having had a Wassermann, and if still in doubt because of the possibility of the coexistence of the two diseases it becomes our duty to excise a single gland for pathologic examination.*

The following cases, which were operated by other surgeons as tuberculous cases afterward came under observation at our clinic, and *cleared up* (after a positive Wassermann was obtained) under proper medication.

CASE E. J. Colored female, age 23.

*Clinical Diagnosis.*—Tuberculous cervical adenitis.

She has noticed a swelling in her neck for four weeks. Pains and night sweats. Cough.

*Examination.*—Enlarged mass under right sternomastoid, near its origin; mass is the size of a hen's egg. Mass is hard, other glands involved. Wassermann positive.

She was operated at the Charity Hospital. A large chain of glands were removed from one side of her neck, the diagnosis there being clinically the same made by us,—tuberculosis. When the glands appeared in the other side of her neck, *she was given two doses of salvarsan at our clinic. The glands disappeared. She has gained in weight and there have been no recurrences.*

CASE O. W. Colored female. (Fig. 15.)

*Diagnosis.*—Tuberculous cervical adenitis.

About one month ago she noticed that the glands below the left side of jaw began to swell, and after two weeks she went to a doctor who "lanced" them. After this procedure, the mass increased in size and continually discharged.

*Past History.*—About one year and a half ago she noticed a swelling on the right side of her neck. She was operated by Dr. A. About three months ago she noticed the swelling on the left side of her neck. One miscarriage. One living child.

*Examination.*—Multiple scars on neck, both sides. There are many circumscribed masses in both sides of neck, which are movable under the skin. On the left side of the neck there are some of the glands which are matted together and show a tendency to break down, some periadenitis. The epitrochlear glands are not enlarged. From some of the sinuses of the neck there is a watery discharge, some flocculi in the discharge. Von Pirquet markedly positive. Wassermann positive (three plus). July 7, 1917, 6 decigrams salvarsan given.

CASE L. D. Age 35.

*Clinical Diagnosis.*—Tuberculous cervical adenitis. Wassermann positive.

Four years ago the patient had a swelling on the right side of her neck, which would enlarge during the winter, and during the summer months the swelling would diminish in size. Three weeks ago the neck began to swell again.

*Examination.*—There is a diffuse swelling, redness about three inches in diameter on the right side of the neck, involving the region of the angle of the jaw. There are two masses, one larger than the other and a granulating “sore.” On pressure the masses are painful to the touch, they are hard, except in the upper portion of the larger mass, which feels slightly fluctuant. Wassermann positive (three plus).

These observations are not intended to enter a denial of well-established facts regarding the greater frequency of tuberculosis of the cervical glands, *but rather to emphasize the frequency of syphilis as a cause of hyperplastic lymph gland masses in the neck.*

Lymph gland enlargements due to syphilis are found in any of the triangles of the neck, but especially have we noted a greater frequency under the sternomastoid and above the omohyoid.

The glands vary in size from the slightly enlarged gland, to masses extending from the tip of the mastoid almost to the clavicle. The mass is usually painless, but at times there is some pain complained of by the patient. Contrary to the opinions of some, *peradenitis is present*, causing a matting together of the glands to such an extent that the mass feels like a single tumor.

*The degeneration of the mass with sinus formation as noted before must not be overlooked as evidence of syphilis.*

*The majority of cases have presented no neighborhood lesions such as chancre of the lip, tongue, tonsil, or mucous patch or gumma of the buccal cavity. The absence of the history of an initial lesion was often noted, even when noted it was many years removed.*

The majority of cases presenting these large masses limited to one side of the neck occurred in adult negro males.

The absence of a primary growth, the age of the patient, the relative absence of pain and the good general health of the patient help to exclude malignant disease.

The clinical laboratory helps to eliminate tuberculosis and Hodgkin's disease by returning a positive Wassermann and a negative blood picture for tuberculosis and Hodgkin's disease.

The masses due to syphilis promptly respond to proper anti-syphilitic medication; within a week the mass begins to melt away.

The following histories and photographs are presented to support the statements above.

CASE E. L. Colored male, Feb. 11, 1915. (Fig. 16.)

*Clinical Diagnosis.*—Gumma of neck.

Swelling in the right side of neck.



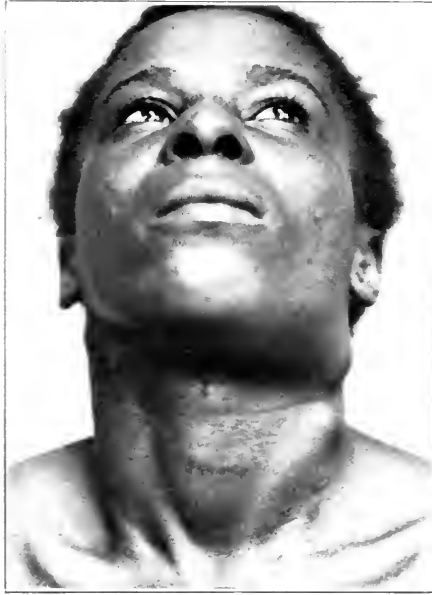


Fig. 15.—Chronic adenopathy. Wassermann  $+++$ , von Pirquet  $+$ .

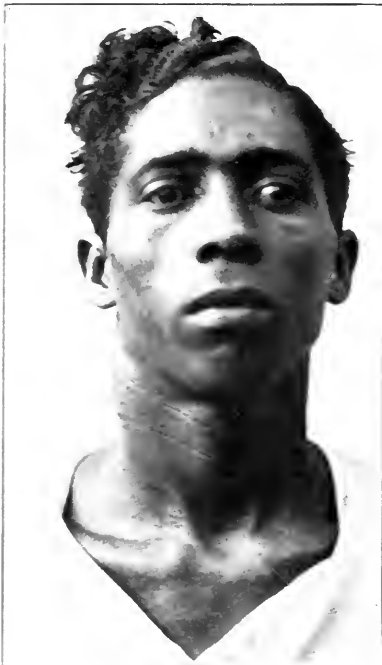


Fig. 16.—Chronic adenopathy. Wassermann  $--$ .

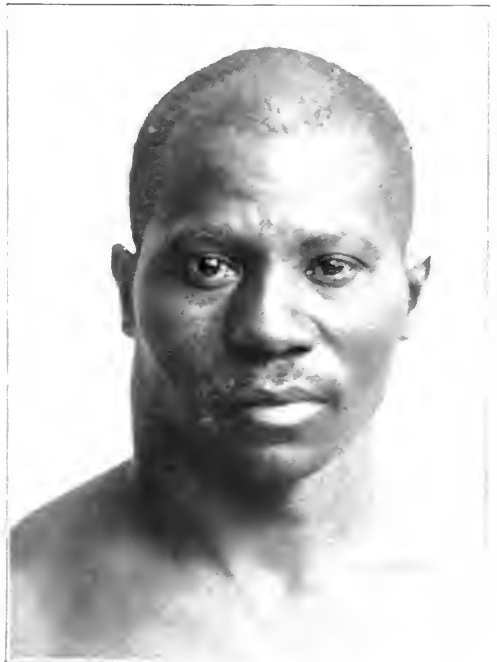


Fig. 17.—Syphilitic adenitis.



*Past History.*—He was treated by Dr. E. for "rheumatism" during September, 1914. He had a cough recently. Ten years ago he had a sore on his penis. Eruption on body, two months later. He had joint pains, principally at night. Treatment improves his condition.

The swelling in his neck is not painful, except when he swallows or coughs. He does not think that he has had fever recently.

*Examination.*—On the right side of his neck there is a large mass, which occupies the position of the sternomastoid muscle as far down as the thyroid cartilage. The mass is hard, it is not attached to the skin, it is nodular, movable, painless. The glands of both sides of his neck are palpable. The epitrochlear glands are large and painless. The skin of his neck and chest are covered with seborrhea. Tonsils are not enlarged. There are no mucous patches in the mouth. Rigg's disease. Wassermann positive (three plus). February 13. Greatly improved.

CASE L. Colored male, age 39. (Fig. 17.)

*Clinical Diagnosis.*—Syphilitic cervical adenitis.

He first noticed a stiffness in his neck about one month ago, then a mass appeared in the neck, which has grown since. He has pain at night. There are no other swellings.

Previous history of luetic infection. Alopecia.

On the right side of his neck there is a prominent mass, the apex of which is about one inch below the angle of the jaw. The mass extends downward to the supraclavicular space. The "mass" is made up of hard discrete, elliptical masses. The left cervical glands and epitrochlear glands are enlarged. Wassermann positive (three plus).

CASE T. B. White male, age 30. (Fig. 18.)

*Diagnosis.*—Syphilitic cervical adenitis.

Nine months ago he first noticed a small mass on the left side of his neck. This mass has increased rapidly in size during the past two months. Recently he has noticed difficulty in swallowing.

*Examination.*—On the left side of his neck there is a mass which extends from the mastoid to the clavicle, the greatest prominence of the mass is in the supraclavicular triangle. The mass is made up of discrete glandular masses, which are hard. No pain on palpation, no sinuses.

No similar enlargements anywhere else on his body. The mass is not adherent to the skin. Sore on penis six years ago, he has never had any secondaries. Wassermann positive (three plus).

CASE S. B. Colored female, age 17. (Fig. 19.)

*Clinical Diagnosis.*—Multiple superficial gummata. Cervical adenitis.

Nine weeks ago the left side of her face began to swell, the right side has recently begun to swell. She had no pain in her face. On the right side of her face there are evidences of old scars from previous ulcerations particularly under the angle of the jaw and ear. On the left side of her neck there are several hard, discrete masses extending from the tip of the mastoid, down to the

angle of the jaw and then seem to follow the outline of the jaw. In this same region we find irregularly shaped, undermined edges, ulceration. Wassermann positive.

CASE C. E. Colored female, January 21, 1915.

*Clinical Diagnosis.*—Syphilis; mucous patches on tonsils; cervical adenitis.

She has not had any pain, but has noticed in the mirror that both tonsils were white. There has been some difficulty in swallowing for several days.

*Examination.*—Large mucous patches on both tonsils. The cervical glands are enlarged, discrete, and nonadherent to the skin.

CASE P. L. Colored female. (Fig. 20.)

*Diagnosis.*—Syphilitic cervical adenitis.

Swelling in left side of neck for three weeks. Pain at night. Chills and fever, pains in her chest.

*Examination.*—Fairly well nourished.

On the left side of her neck just under the tip of the mastoid there is a large, hard, circumscribed, movable mass, which seems to have no deep attachments. All cervical glands along the trapezius are palpable, there are palpable glands on the right side of the neck as well. Epitrochlears are palpable. Wassermann positive.

CASE C. A. White male, Jan. 2, 1915.

*Clinical Diagnosis.*—Syphilitic cervical adenitis.

For the past two months he has noticed a large "lump" in the cervical region (left). No pain at any time, no fever, no similar masses on body. Six months ago he had a sore on penis. Three months ago he had a general papular eruption.

*Examination.*—There is a generalized papular eruption and a general glandular enlargement. Particularly in the left cervical region, there is a mass which is hard and nonadherent to the skin. No evidence of inflammatory reaction.

CASE E. B. Colored female, age 16.

*Clinical Diagnosis.*—General adenopathy lues.

Four months ago she noticed a soreness in her mouth, pains in her legs, swelling of the legs, restlessness at night. Loss of appetite. She says that the glands below the ear were the first to swell.

*Examination.*—The glands on both sides of her neck are enlarged, painless, and discrete. Enlarged glands in left axilla and in both inguinal regions. Total leucocyte count 9950. Lymphocytes 24 per cent, endothelial leucocytes 6 per cent, neutrophils 70 per cent. Wassermann, positive (three plus).

CASE M. H. Colored female, age 24 years.

*Clinical Diagnosis.*—Cervical adenitis syphilis.

Referred by Dr. L. "to determine the cause of the swelling."

One week ago she noticed a swelling in her neck on the right side, pain only when she swallows. She has "light fever." Has been confined to bed only one day. There has been some difficulty in swallowing for two months.



Fig. 18.—Syphilitic cervical adenitis.



Fig. 19.—Syphilitic cervical adenitis.

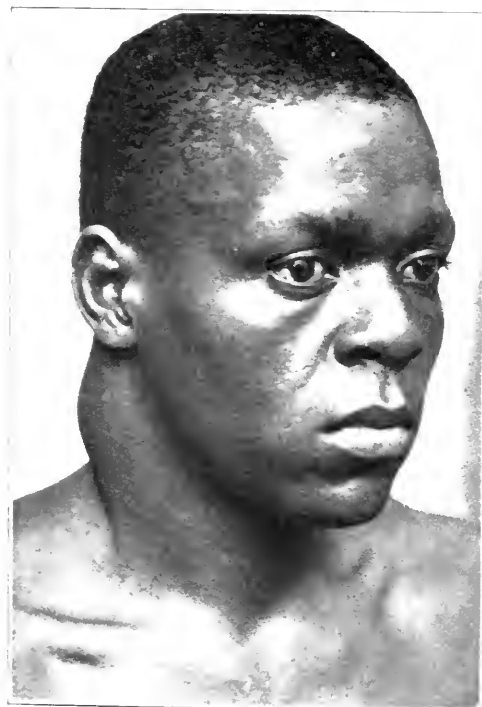


Fig. 21.—Cervical gland enlargement due to syphilis.



Fig. 20.—Syphilitic cervical adenitis.



*Examination.*—There is a mass in the right supraclavicular space, which is nodular, not adherent to the skin, only slightly movable, painless, no glandular enlargements anywhere else. Has had one premature delivery and two children that died soon after birth. Wassermann three plus.

CASE A. McC. Colored male, age 28 years, June 10, 1916.

He has noticed a knot on the right side of his neck for three weeks. The mass is getting larger, there is pain in the region of the mass. Three months ago he had a similar, but smaller, mass in the right supraclavicular space. This case was operated by Dr. S. Five years ago he had a venereal sore.

*Examination.*—On the right side of his neck along the posterior border of the sternomastoid muscle there are several hard, discrete, glandular enlargements. They are movable, not painful, June 13. There is a mass, about three by two inches in the right cervical region posterior border of the sternomastoid. There is marked periadenitis. The mass is adherent to the skin. It is movable on the underlying soft parts, but is adherent to the skin. There are no areas of shortening. Wassermann three plus.

CASE C. M. Colored male, age 18 years.

*Clinical Diagnosis.*—Syphilitic cervical adenitis.

Eight months ago he had a chancre. Right tonsil is enlarged. Buccal mucosa is normal. In the left cervical region there are several prominent masses, the most prominent is about one fingerbreadth below the border of the body of the jaw, and another in the supraclavicular triangle. Masses are movable under the skin, nodular, hard, and not painful. Epitrochlears are enlarged as well as the axillary and inguinal glands. Wassermann positive.

CASE F. G. Colored male, age 26. (Fig. 21.)

He woke up one morning about five months ago and found a small lump in his neck which he attributed to sleeping on high pillows. Pain was noted in the beginning. The mass has steadily increased in size, it is only painful when pressure is applied. He has a slight cough, has lost 21 pounds during the past six or eight weeks.

Five years ago he had a sore on his penis. For about three months following the sore his joints would be stiff in the mornings.

*Examination.*—Fairly well nourished. There is a large, movable, hard mass under and posterior to the sternomastoid muscle, the mass is about the size of a small orange. There is a general glandular enlargement, varying in size. Wassermann was requested, but the patient did not have it taken.

#### CONCLUSIONS

(1) When a neck mass presents itself, the many possibilities must be considered before jumping at conclusions.

(2) The clinical laboratory should be utilized early if many of these cases are to be benefited by treatment of any kind.

(3) Congenital cysts are to be differentiated from tuberculous glands, in children especially.

(4) Carotid body tumors must be considered if a patient presents himself with a painless, nonpulsating, firm mass occupying the course of the carotid artery.

(5) A history of the mass having been present for several years is suggestive of a carotid body tumor.

(6) Primary neoplasms of lymph glands are most often of the round-celled sarcoma type.

(7) Hodgkin's disease is often mistaken for other conditions.

(8) The diagnosis is dependent on clinical laboratory findings.

(9) Tuberculous cervical adenitis and hyperplastic gland masses due to syphilis are often confused.

(10) The removal of a single gland for examination, the Wassermann, and other laboratory methods will avoid many needless cervical adenectomies.



## TATTOOING AND SYPHILIS

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A THOROUGH understanding of the relationship of tattoo marks to inflammatory reactions of the skin would undoubtedly throw light on the mechanism of inflammation. The reactivity of the body as a whole, as well as that of the individual cell, is intimately associated with the influences which determine the location of lesions and upon this reactivity depends the effects produced by the more or less accidental introduction of irritants, such as micro-organisms, chemicals, and foreign bodies, and by traumatism.

It is well recognized clinically that irritation and trauma often determine the location of, and lay the foundation for, secondary and tertiary syphilitic lesions. As instances of this may be mentioned the development of periostitis with greater frequency along bones superficially situated than in those more protected by overlying soft parts; the occurrence of particular types of lesions in localities subjected to the binding of clothing such as the corona veneris; the irritant action of highly seasoned foods, nicotine, etc.; and traumatism resulting from carious teeth in the production of buccal mucous syphilides; and the occurrence of condylomata, in localities subjected to the combined irritant action of heat, friction, and maceration. Similarly localization of syphilides may be determined by exposure to great heat alone, as seen in the appearance of a syphilitic roseola on surfaces where it ordinarily rarely occurs, as for instance on the faces of cooks, stokers, etc. Tarnowsky<sup>1</sup> in 1877 demonstrated experimentally the occurrence of syphilides following the local application of irritants to the skin. Abrasions of the skin, insect bites, wounds, etc., in syphilitics not infrequently are complicated by a subsequently developing syphilitic inflammation.

A great deal could be said concerning the participation of syphilis in the pathology of other diseases occurring simultaneously with syphilis. This is frequently most beautifully illustrated in the

commoner types of dermatoses, when they occur on the skin of syphilitic individuals. It is probably true that the condition of the skin in syphilitics described as "allergy" predisposes to skin diseases, but it is a matter of frequent observation that the development of the dermatoses is the determining factor in the localization of syphilitic inflammation, which changes and tends to obscure the original characteristics of the lesion. Specific instances occur frequently in the literature, for instance, Bettmann<sup>2</sup> mentions the association of syphilis with the lesions of psoriasis.

In what respect these phenomena simulate or differ from that of the localization of syphilitic deposits in tattooed areas of the skin can only be surmised. It seems not unreasonable to suppose that the particles of pigment deposited in the cutaneous tissues constitute an irritant either by their chemical action or as a foreign body or in both these senses, and it is more than likely that all pigments do not have an equally irritant action, while at least one of them, cinnabar, seems to possess in addition, a protective property. The traumatic element of tattooage must also be considered in association with the probable irritant action of pigment particles, because this alone would influence the local conditions by disturbing the normal relations in the skin.

The influence of tattooing in localizing dermatoses other than syphilis is seen occasionally in leprosy<sup>3</sup> and erysipelas,<sup>4</sup> Ullmann<sup>5</sup> reported the occurrence of granulomatous nodules about particles of cinnabar in a case tattooed in red and blue fifteen months previously.

We wish to present a striking instance of the influence of tattooing on syphilitic eruptions in a case studied by us in the Syphilis Clinic of the Johns Hopkins Hospital.

P. G., a white man forty-eight years of age, formerly a pugilist, but now a ship's stoker, came to the clinic on December 14, 1916, complaining of sore throat and breaking out. In 1908 he had been extensively tattooed over the chest and arms. On June 8, 1916, he developed a chancre on the penis eleven days after exposure. The chancre disappeared in a few days under local treatment with Black-wash and iodoform. About six weeks later, July 18, he noticed an eruption on the chest which later spread over the entire trunk and extremities, and has remained until the present time. On

the first of October his throat became sore, increasing in severity until now. Condylomata about the anus made their appearance December 1. No malaise, headache, or osteocopic pain.

*Examination.*—Undersized, robust man with “cauliflower” ears and depressed fracture of nasal bones acquired in pugilistic bouts. Pupils regular, the right larger than the left, both reacting sluggishly to light but well during accommodation. Very extensive papuloerosive lesions on the buccal mucous membrane, extending into the pharynx as far as can be seen. The voice is very low and husky, and deglutition is difficult and exceedingly painful. Tonsils markedly enlarged. Exceptionally pronounced general glandular enlargement, the superficial glands being everywhere visible as small tumors beneath the skin. Heart, lungs, and abdominal viscera apparently normal.

*Genitals.*—On the inner lamella of the prepuce is the indurated scar of a healed chancre; scrotum and contents normal. Deep reflexes active throughout and equal on the two sides.

*Skin.*—The skin over the chest, epigastrium, arms and forearms is beautifully tattooed in blue-black, green, and two shades of red. The designs and decorations were skillfully outlined and beautifully executed, and represent, as shown in the illustrations, Figs. 1, 2, 3, and 4, an eagle alighting in the top of a dead tree in the act of devouring a heart, with eight smaller birds hovering in the air about him. About the patient’s neck is a garland of flowers and leaves, with a butterfly in the episternal notch. Over each deltoid is a partly opened Japanese fan partly encircled by a rose and sprays of leaves. On each arm is a serpent, while a Scottish Highland girl is on the left and a Japanese girl on the right arm. Each forearm is decorated with a dragon and symbolic designs.

Distributed over the extremities, especially on the extensor surfaces are numerous typical pinhead-sized round, to dime-sized flat, scaly papules, with a tendency to become confluent, and in places forming annules. There are a few similar widely scattered papules on the trunk. Where the eruption occurs in the tattooed areas, it is sharply localized in portions of the designs, except on the forearms where it extends from the decorations out upon the untattooed skin, and shows marked tendency to become confluent. Wassermann reaction positive.

The localization is especially well shown in Figs. 2, 3, and 4. In Fig. 2 is shown the fan in the left deltoid region. This decoration is executed entirely in blue-black. Along the anterior margin of the design sharply circumscribed within the blue-black line, and extending a short distance along the shoreline of the pictorial decoration of the fan, is an almost unbroken band of confluent, strikingly elevated, rounded papules. This margin is very deeply pigmented with China ink, so that the papules are black, and have an appearance not very unlike that of keloids in a negro. Where the spray of leaves on the anterior aspect crosses a vaccination scar, there are three small papules on the blue-black stem. There are no papules on the petals of the rose which is done in cinnabar, but on two of the large leaves done in China ink, there are several. A single small papule is seen in the line forming the posterior margin of the fan.

Lower down on the same arm (Fig. 3) is the figure of the Scottish Highland girl done in blue-black and two shades of red; a bright red, which is cinnabar, and a dark somewhat purplish red, the nature of which was not ascertained, but probably is carmine. In the blue-black hair and lines marking the features of the face and in the blue-black bodice, several fairly large papules can be seen, especially well localized in a deeper shaded band about the arm, and in the lines forming a buckle on the braid which passes over the shoulder of the figure. Down the front of the figure is a plaid design in which the lines and solidly colored squares are done in cinnabar. Compared to the rest of the skirt, this portion is relatively free of eruption, there being but a few papules at the top and bottom. The checkered portion of the skirt, done in lines alternating blue-black and dark purplish red, is the seat of a most intense eruption. While the papules are more numerous in the blue-black lines, they are very much more numerous in the dark red than in the cinnabar tinted portions of this and the other tattooed figures. In fact, this figure contains the only instance of papules occurring in the cinnabar coloring. The blue-black shoes also show a striking localization.

The serpent shown in this picture and also in Fig. 4 is particularly interesting. It is done in the four colors. The checks representing the striped belly are cinnabar. Only one small papule is seen on the belly, and that is in the white square of otherwise nor-



Fig. 1.—Pt. P.G. Illustrating extent of tattooing and distribution of syphilitic rash.



Fig. 2.—Pt. P.G. Illustrating lineal localization of the rash in the deeply pigmented blue-black margin of the fan.



Fig. 3.—Pt. P.G. Showing striking localization in the figure of a Scotch Highland girl, and in the eye and spots of a serpent.



mal skin, and just touches the adjoining red square. Similarly the body of the serpent which, with the exception of the spots marking the back, is done in blue-black, is almost entirely free of eruption, only the lower one-third containing papules. In sharp contrast to this the spots which are done some in dark red, some in green, and some in deeply pigmented blue-black are frequently completely occupied by papules which do not extend beyond their margins, and all three colors are involved. In the lower end of the serpent, with the exception of the cinnabar, all colors and the untattooed skin are involved in the eruption with any localization. In Fig. 4 a swallow on the side of the patient can be seen to contain a group of papules in each wing which are much larger and more elevated than the several widely scattered single papules on the untattooed skin in this vicinity.

The decoration on the lower arm is a dragon done in blue-black and cinnabar, and although the eruption is massed in most of the blue-black portion with the localizing feature above, the lower portion is not so characteristic. Toward the distal part of the patient's lower arm the rash is so much more intense than elsewhere that the untattooed skin comes in for a larger share of the disturbance. The apparent ability of the cinnabar pigment to inhibit the formation of papules, however, is for this very reason nowhere more strikingly illustrated than in this figure, because even here it is entirely free. The eruption which everywhere else overruns the figure and adjacent skin stops abruptly, not only where the cinnabar is present, but fails to invade the areas of untattooed skin surrounded by cinnabar tinted areas. This is seen along the belly of the figure which is marked by alternating squares of normal skin and cinnabar pigmented skin, running along the right-hand margin of the figure. At one point the blue-black thigh of the dragon's left hind leg crosses this margin. On both sides of the margin it contains papules, but at the point of crossing there is none.

There were numerous other instances of localization of the rash in the tattooing that were just as striking as these mentioned, but it seems unnecessary to multiply these examples in the description. Unfortunately, after receiving an injection of diarsenol on his second visit to the clinic, the patient failed to return, so that opportunity for further study of the case was lost.

During the past year we have carefully examined a very large number of syphilitic individuals bearing tattoo designs, but have failed to observe a single instance of selective localization of syphilides in them. Two cases, one done in blue, and one in blue and red were seen with several single papules in blue-black coloring, but in these instances we were convinced that the location of the papules was a pure coincidence, there being nothing to distinguish them from papules elsewhere on the untinted skin. In no instance have we seen in the clinic, or been able to discover in the literature examples of intensified syphilitic disease in lymph glands draining a tattooed area, although these glands are known to contain pigment from the area.

Tattooage is performed by puncturation or wounding of the skin with solid or hollow needles and by introducing into the skin in this manner, various pigments. The needles are usually ordinary sewing needles, attached to wooden handles in bundles of two or more, although the finest polychrome work requires the use of special hollow needles. In general, the procedure is to outline the design on skin either by puncturation after moistening the needles and dipping them in the pigment, or by drawing with the pigment moistened with water, and puncturing along these outlines. In a similar manner the design is filled in with one or more colors. Sometimes, after puncturation, the artist moistens his finger, dips it in the pigment and rubs the pigment into the puncture wounds. Various fluids are used for moistening the pigments, boiling water being regarded as best, but sometimes a tattooer will moisten the pigment with his own saliva, spit upon the design to rub in the pigment, or put the needle bundle into his mouth to suck out the pigment when going from one color to another.

The most frequently used pigment is carbon, usually in the form of India ink. Lampblack and gunpowder are occasionally used. These black pigments produce a blue color in the skin. Cinnabar (mercury sulphide) and carmine (preparation of cochineal) are used for shades of red. In the skin cinnabar produces a vermilion, and carmine a deeper purplish red. Some of the other pigments used, but less frequently, are native copper carbonate (malachite green) for green, indigo and Prussian blue for blues, gold powder, silver powder, etc.





Fig. 4.—Pt. P.G. Showing rash localizing itself in tattoo figures of arm and forearm.

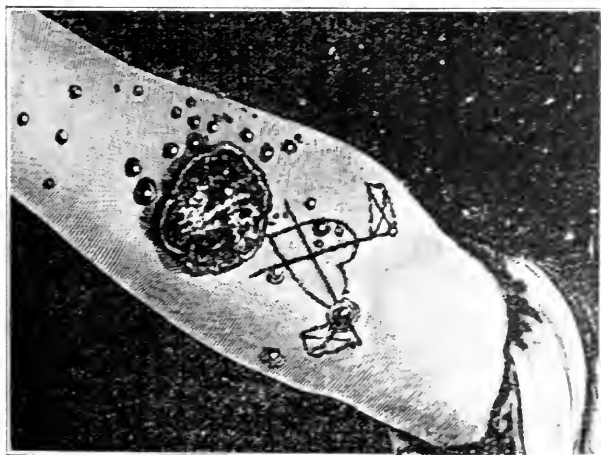


Fig. 5.—Case reported by Dore of cutaneous infection with tuberculosis by tattooing. The primary lesion is a large mass below the heart in the design. The small scattered pustules developed after application of a wet dressing.



Following tattooage, there is more or less inflammation with swelling, for some hours. In the ones tattooed with cinnabar, this reaction is more intense, the inflammation sometimes lasting for days, with a sensation of itching after healing which may last for months. When saliva is used, severe inflammation usually follows and is sometimes accompanied by erysipelas, gangrene, suppurating buboes, and inoculation with tuberculosis<sup>6</sup> (Fig. 5), and syphilis (Fig. 6).

The pigments are deposited for the most part superficially in the corium where the particles become ingested by phagocytic cells, very few remaining in the intercellular spaces. A large part of the pigment is carried by the lymphatics to adjacent lymph glands. The intracellular particles remain almost indefinitely with a very slight gradual disappearance. Very old tattooing sometimes has become blurred by this process. No pigment remains long in the epidermis. A very slight mononuclear infiltration of the corium persists after the acute reaction subsides.\*

Accidental inoculation with syphilis during tattooage was at one time much more frequent than it is today. Moistening the pigments and needles with the tattooer's saliva, and rubbing in the pigment, made the inoculation almost certain when the tattooer had mucous syphilides in his mouth at the time. Descriptions of individual cases and small epidemics occur in the literature. The earliest reference which we were able to find was in 1853, when Hutin<sup>7</sup> mentioned one case. Two subsequent articles by Joslas<sup>8</sup> and by Robert,<sup>9</sup> in 1877 and 1879, we were unable to consult because we could not gain access to the periodicals in which they were published. Maury and Dulles,<sup>10</sup> in 1878, described a small epidemic in which fifteen individuals tattooed by one man, developed chancres in the tattooing, only four nonsyphilitic and three syphilitic cases escaping without chancres. Of the fifteen cases inoculated, ten developed multiple chancres ranging in number from two to forty-one. The tattooer at the time of the sittings had buccal mucous patches and anal and scrotal condylomata. In mixing the pigments he always used his saliva for the cinnabar and not for the India ink, although occasionally he rubbed in both with saliva, and also put the needles in his mouth. The authors do not specify in all cases the color in which

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\*For a fuller description of the histology of tattooing, see article by Dohi.<sup>20</sup>

the chancres appeared, but in two cases they developed in both, and in two others in the red alone. These four cases all had multiple chancres. Uniformity of the secondary lesions are striking. Twelve developed buccal patches, twelve genital, twelve plantar, and ten palmar syphilides, and ten condylomata.

In 1886 Arthur<sup>11</sup> cites a communication from T. K. Wilcox in which are mentioned twenty-six cases of primary syphilis following tattooing by an individual who had buccal mucous patches and constantly moistened his needles with his saliva. Similar outbreaks of tattoo-syphilis are described by Whitehead,<sup>12</sup> Barker,<sup>13</sup> Cheinisse,<sup>14</sup> Thomas,<sup>15</sup> and Zechmeister.<sup>16</sup>

Although inoculation with syphilis through the process of tattooing had been reported in 1853, the earliest description of the occurrence of syphilitic rashes in tattoo marks that we were able to find is a publication by Zechmeister<sup>16</sup> in 1901. Since that time we found only eight additional reports, totaling in all fifteen cases, three of which were not sufficiently definite to preclude the possibility of coincidence as a serious consideration.

Zechmeister cites a case observed by Rona in which an early generalized syphilitic rash had become greatly intensified in a tattoo design, and another case seen by Plummert which exhibited a generalized recurrent papular rash becoming confluent over the whole tattooed area (Fig. 7). Wechselmann<sup>17</sup> reported a case with generalized macular rash. The macules surrounded on all sides a tattoo mark, while the tattoo mark was elevated above the surface by papular lesions in a manner which threw the complete design into relief. He describes also a case in which an attempt had been made to remove the tattoo mark so that the design was obliterated. A subsequently acquired secondary syphilitic eruption was so intensified about the few remaining pigment particles that the original tattoo design was reproduced in papular outlines. Lipschütz<sup>18</sup> reports a case in which a recurrent syphilitic rash was sharply localized in tattooing, and occurred nowhere else on the skin. In three cases reported by Holland<sup>19</sup> the localization feature was not so striking, but in a fourth case there was definite selective localization. Dohi's<sup>20</sup> publication of a very striking case is interesting particularly because of the very thorough manner in which the case was studied, and for the completeness with which the whole subject

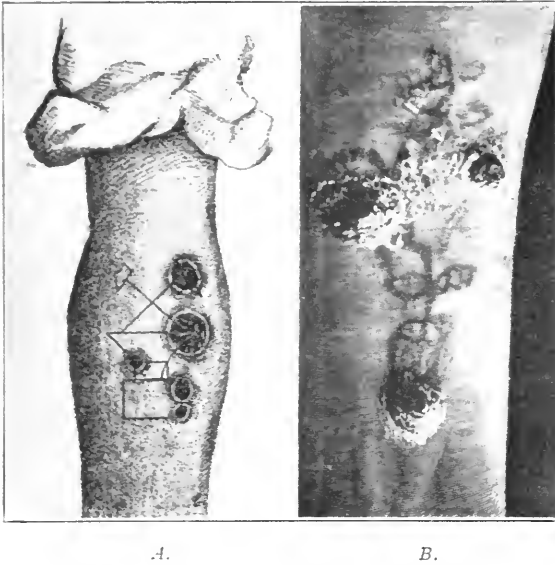


Fig. 6.—Multiple chancres developing in tattooing following inoculation with saliva of a tattooer with buccal syphilides. *A.* Case reported by Cheinisse. *B.* One of several cases reported by Barker.



Fig. 7.—Plummert's case reported by Zechmeister, showing a recurrent rash developing in a tattoo mark two weeks after tattooage.

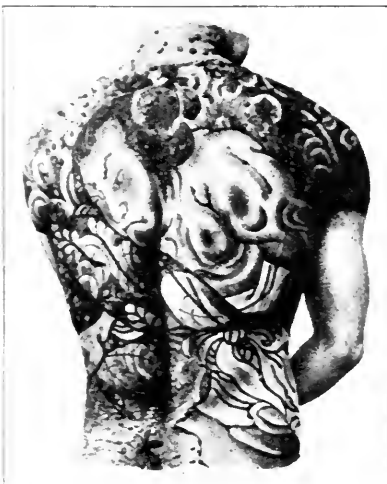


Fig. 8.—Case reported by Dohi, showing localization of syphilitic papules in the lines of an extensive tattoo design done sixteen years prior to infection.



Fig. 9.—Case reported by Bernheim and Glück, showing a recurrent syphilide in an old tattoo mark which had been embellished by recent additional tattooing. The outbreak occurred in the newly tattooed areas two weeks after tattooage.



is presented. In his article we found the first serious attempt at an analysis of the factors underlying the interesting action of cinnabar. We obtained from his article many of the references from which we quote. In his case the syphilitic papules occurred in the blue lines and were more numerous in the heavily shaded blue areas. No papules occurred in the cinnabar tinted areas (Fig. 8). Two cases reported by Florange<sup>21</sup> are similar, but differ with respect to color selection. In an article by Aoki<sup>23</sup> reporting one case, is a description of a very interesting experiment with tattooing and syphilis which the author carried out in rabbits. Tattooage of the scrotum of a rabbit, half in India ink and half in cinnabar, was followed a month later by inoculation with material rich in *T. pallida*. In the blue area an ulcer rich in treponemata appeared, while the red area remained unaffected. He repeated the experiment with the same result.

In an entirely unique case described by Bernheim and Gluck<sup>23</sup> the tattooing was not involved in the first outbreak of secondary syphilis. After a course of treatment the patient allowed the old tattooing to be embellished by the addition of draperies done in cinnabar. Two weeks later, the new lines became the seat of sharply limited, crusty, recurrent syphilides (Fig. 9).

We were unable to have translated a Japanese article by Kurita.<sup>24</sup>

No very comprehensive analysis of the cases reported is attempted because of lack of uniformity in the presentation of data, and furthermore, with the exception of Dohi's case no attempt to study cases intensively is manifest. In the case which we report, this criticism applies as well, because, as already stated, the uncooperative attitude of the patient defeated our plans. The patient's condition was such as to make immediate treatment imperative, and as soon as he experienced the relief which one injection of diarsenol afforded, he neglected his promise to return to the clinic, and could not be traced.

Sufficient evidence is presented, however, to establish beyond peradventure that there is a definite selective localization of syphilitic deposits in tattooing. That this occurs more frequently than the limited number of cases reported would indicate, is highly probable, but that it is a rare phenomenon is borne out by our experience and that of other investigators. It may occur with the advent of

sypphilis in previously tattooed individuals, the outbreak being of an early secondary type, as well as in those syphilitics who resort to this form of cosmesis after infection. Among the former tattooage may have been performed as much as sixteen years previously, shorter intervals being the rule; but when performed on syphilitic skin, the interval preceding the outbreak is very short\* and the lesions are of a late recurrent type.

When present, the localization is almost invariably in carbon (blue-black) pigmented skin. When other colors are employed they seem to participate to a similar extent in the outbreak, with the notable exception of cinnabar. Instances of localization in vermilion (cinnabar) tattooing, however, are reported, and also instances of chancres following tattooage inoculation when this pigment has been moistened with the saliva of the syphilitic tattooer.

Comments and explanatory views on these phenomena cover a wide range. Practically all authors agree that all pigment particles in the skin constitute an irritant, but they disagree on the nature of the irritant action. Most ascribe a chemical action to cinnabar and compare the action of carbon to that of an inert body. Others regard the action of the pigment particles as productive of areas of lowered resistance without attempting to specify the mechanism by which this is accomplished, and ascribe different degrees of activity to the various pigments. By a few, the mercury ion of cinnabar is held responsible for activity both as an irritant and as a therapeutic protector. They believe the mercury is slowly split off for a very long period, producing irritation by its chemical action on the surrounding cells, and retarding the development of treponemata by its well-known therapeutic property. But the altered local environment produced by irritation which might favor the growth of treponemata is more than offset by the therapeutic action which retards, though it may not destroy them. This margin of antiseptic activity is greatest in freshly tattooed areas, but is greatly reduced after the particles have become incorporated in the phagocytic cells and is finally lost entirely in time. Positive and negative chemotactic influences of various pigments on the treponemata and on leucocytes have been mentioned, but so far as we know have not been suggested as probable explanations.

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\*Two weeks in two cases in which the interval was noted.



All these views find confirmation in some cases and contradiction in others. We believe the influences of tattooing on syphilis of the skin are several and varied. Undoubtedly, local environmental conditions must be altered to favor the growth of the syphilis treponemata, at the expense of the protective mechanism of the skin, before the local eruption can be intensified, because there is no criterion for supposing that this defensive mechanism would be augmented by influences such as wounding the skin and the introduction of foreign particles represented by tattooing. The question then is what are the factors in tattooing that alter the local conditions. In order that they may be more accurately scrutinized, let us first state a general conception of the mechanism of infection and resistance as it applies to syphilis.

Syphilitic infection begins with the multiplication of the treponemata in the body; syphilitic disease does not follow until there is a reaction to the invader on the part of the host. During this interval the treponemata multiply and invade the body by creating for themselves suitable environments for their growth. The varying cultural conditions in different tissues offer the organism an opportunity for selecting the most favorable environment for its growth and maintenance. That the treponemal invasion may progress without opposition may be because of the organism's insolubility and consequent lack of irritating action. Theobald Smith<sup>25</sup> places the *T. pallidum* in a class of organisms "which may dispense largely with both offensive and defensive processes." He says "we can conceive of this type as exerting a metabolic activity approximating so closely to that of the host that the latter reacts but slightly and then only after a long period of stimulation." When the organisms have increased in numbers to such an extent that the cumulative effect of their irritating powers threatens to interfere with the metabolism of the invaded tissues, the host reacts and a conflict for supremacy ensues. This conflict is marked by tissue and other secondary reactions within the host which become manifest in the type of lesions that are characteristic of syphilis. As long as the treponemata have the upper hand, the conflict endures and the lesions persist. Usually in syphilis the treponemata everywhere gradually lose their supremacy until a balance is struck between their virulence and the protective mechanism of the tissues opposed to them,

and all signs of the battle disappear. But this does not necessarily mean that the treponemata have relinquished their position. On the contrary, they may remain in the environment, reduced in numbers, altered in a sense, in virulence, at bay before an equal opposed force, but equipped to renew the conflict at the first opportunity presenting itself. This opportunity may be furnished by any influence which tends to inhibit or decrease the forces of the protective mechanism of the tissues in the particular environment. We may call this a decreased or lowered resistance to infection.

Anything that interferes with the normal metabolism of tissues will lower their resistance. Irritants and traumatism are the external influences with which we have to deal in this relation of tattooing to syphilis of the skin. That there must be influences from within which determine the susceptibility of the individual to those from without, and that they are very complex must be conceded in order to explain the infrequency with which tattooing has any influence on skin syphilis. Puncturation of the skin of a syphilitic, by causing cell death, produces favorable cultural conditions for the *T. pallidum* and by interference with skin metabolism alters the nutrition of the cells. One tends to increase the virulence of the infection, the other tends to lower the resistance of the cells opposed to it. The deposition of pigments acting as an irritant in the form of a foreign body further lowers the vital resistance of the cells, and the summation of these influences so favors the treponemata at the expense of the tissues that even the protective property of a pigment like cinnabar, which also has a powerfully irritant chemical action, is incapable of opposing the invader. The organisms increase in number until their toxic powers produce a reaction. The skin recovers its resistance and in the meantime a sharply circumscribed local outbreak of the characteristic lesions results.

When a syphilitic infection invades a previously tattooed skin, the conditions are somewhat different. The effect of puncturation could be felt only through the influence of the increased connective tissue elements on the environment, which must be very slight. The irritant action of the pigment particles, which at that time are almost completely phagocyted, must also be slight, but the summation of the two, combined with some influence or influences from within peculiar to the individual at that moment, must so alter the environment

that the organism is given more time and better cultural conditions for growth, while at the same time the pigmented skin through the slight interference with its protective mechanism lacks the same force possessed by the normal skin in opposing the here more virulent invader. Cinnabar, in this instance, probably possesses the dual activity ascribed to it, and its influence will be thrown to either side in the conflict, depending upon which component is the more active. Its irritant action has been greatly reduced by phagocytosis, its therapeutic action may or may not be sufficient to counteract the other influences favoring the treponemata. Its influence will, therefore, depend largely upon the quantitative relationship of these activities.

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## SKELETAL RADIOGRAPHY AS AN AID TO THE DIAGNOSIS OF OBSCURE SYPHILIS

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THE knowledge that syphilis affects the skeletal system is almost as old as definite knowledge of the disease itself. Fallopius, in the sixteenth century, wrote of the bone lesions of syphilis in his treatise, "De Morbo Gallico." Fabricius noted that exostoses were present at birth in certain children affected with congenital syphilis. Jean Astruc, the great French syphilographer, who was born in 1684, gives in his complete work on the venereal disease a wonderfully accurate description of some of the bone lesions of syphilis.

Power and Murphy<sup>1</sup> have well said, "The relation of syphilis to inflammation of the bones has been known for so long a time that the old term 'node,' to denote a local plastic periostitis of syphilitic origin, has passed into folk speech."

We find that Mauriac<sup>2</sup> was one of the first to show that in acquired syphilis bone involvement may be present even at the time of secondary manifestations. From the early beginnings of knowledge of bone syphilis in the times of Fallopius, Fabricius, and Astruc, a great fund of knowledge was slowly acquired from the living, and from pathologic and dissection material. As Sir Jonathan Hutchinson<sup>3</sup> has pointed out, many of the very large irregular and heavy bones in our pathologic museums give evidence of a previous syphilitic inflammation.

It was a number of years after the discovery of the roentgen ray that the far-reaching possibilities of its use in the study of bone syphilis were thought of. Naturally at first radiologists and those clinicians interested in the study of syphilis gave their attention to the radiographic pictures of bones that were suspected clinically of being the seat of specific inflammation, and it was soon found that characteristic changes were apparent, and that specific periostitis and osteoperiostitis gave a definite and characteristic picture.

Keinbock and Hochsinger,<sup>4</sup> in 1901, studied specific bone disease radiographically, and Albers Schönberg, Hahn,<sup>5</sup> Kohler and Ritter added much to radiographic knowledge of this subject. In this country, Ware,<sup>6</sup> among others, and later Nichols,<sup>7</sup> have written on syphilis of the bones from a surgical and radiographic standpoint. Gradually the knowledge of the subject has increased, and it has been noted through the use of skeletal radiography that many bones showed the characteristic radiographic appearance of specific inflammatory processes without any symptoms being manifest,—a silent skeletal syphilis. It has been found, moreover, that in individuals without any specific history these characteristic changes were at times present. Further study of this subject has demonstrated that certain individuals, ailing for years with obscure chronic conditions in which definite diagnoses could not be made, showed definite specific changes in certain bones, which gave the key to an otherwise blind and baffling condition. In these cases a definite history of specific infection seemed entirely lacking. On the other hand, when an exhaustive history was taken and symptoms noted by one who had an adequate knowledge of the more obscure and uncommon signs of syphilis, extremely suggestive facts were noted.

Fournier, in speaking of the dental manifestations of syphilis, has said, "There are erosions and erosions" and so in obscure and latent syphilis, there are "symptoms and symptoms," some of which, to the initiated, will be important, but will be passed by as unimportant by others. The very great importance of skeletal radiography in the diagnosis of syphilis is just beginning to be appreciated, and its use is at present not widespread. It is with no hasty judgment that I say that the Wassermann reaction is a mixed blessing in the diagnosis of syphilis. Despite much clinical evidence and writing, many physicians, specialists, and general practitioners alike still continue to believe that in an obscure case, a negative blood Wassermann reaction rules out syphilis. Many general practitioners still view syphilis in the light of "rashes and mucous patches." They often will say that they do not treat syphilis when at that very time there may be in their consulting room cases of specific aortitis, syphilitic rheumatism, and other obscure manifestations of this disease. Frequently in the reports of operations we find, "There was a negative Wassermann reaction, which ruled out syphilis." A surgeon said, speaking of a group of cases of joint



Fig. 1.—Male, 13 years. Specific bursitis of elbow. Operation. No cure until specific treatment. Followed trauma to elbow. Wassermann negative.





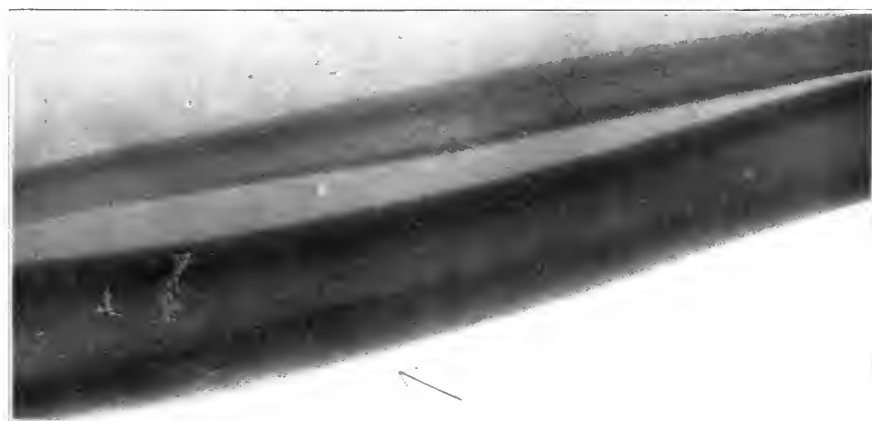


Fig. 2. Male, age 14 years. Juvenile taboparesis. Specific osteoperiostitis tibia. Wassermann positive.



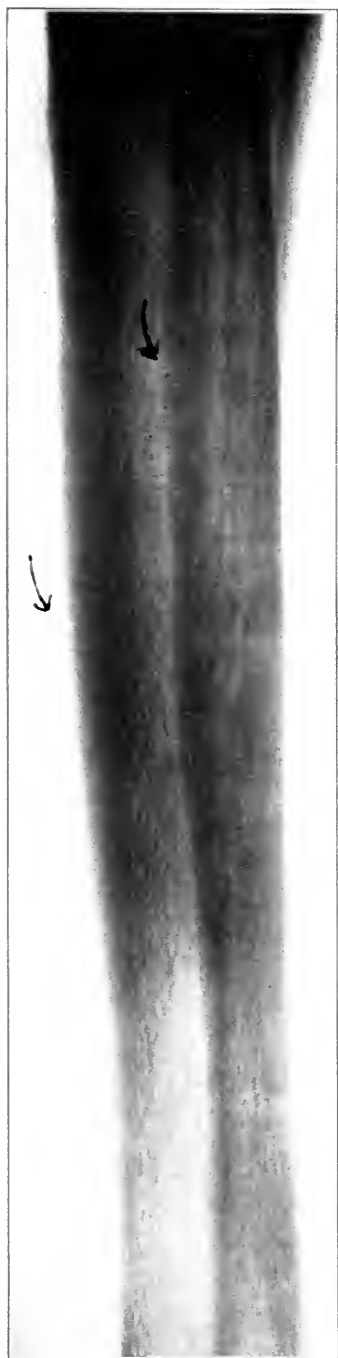
Fig. 3. Male, localized gummatous abscess of ulna. Wassermann negative. No definite history. Resisted proper surgery. Cured in three weeks specific treatment.





Fig. 4.—Male, 44 years. Ulcerated lesion of little finger. Bone involvement. Old specific history. Treated for septic finger. Leg bones show specific periostitis.





A.



B.

Fig. 5.—Adult female. Keratitis. Wassermann negative. A. Specific periostitis tibiae. B. Specific periostitis third metatarsal.



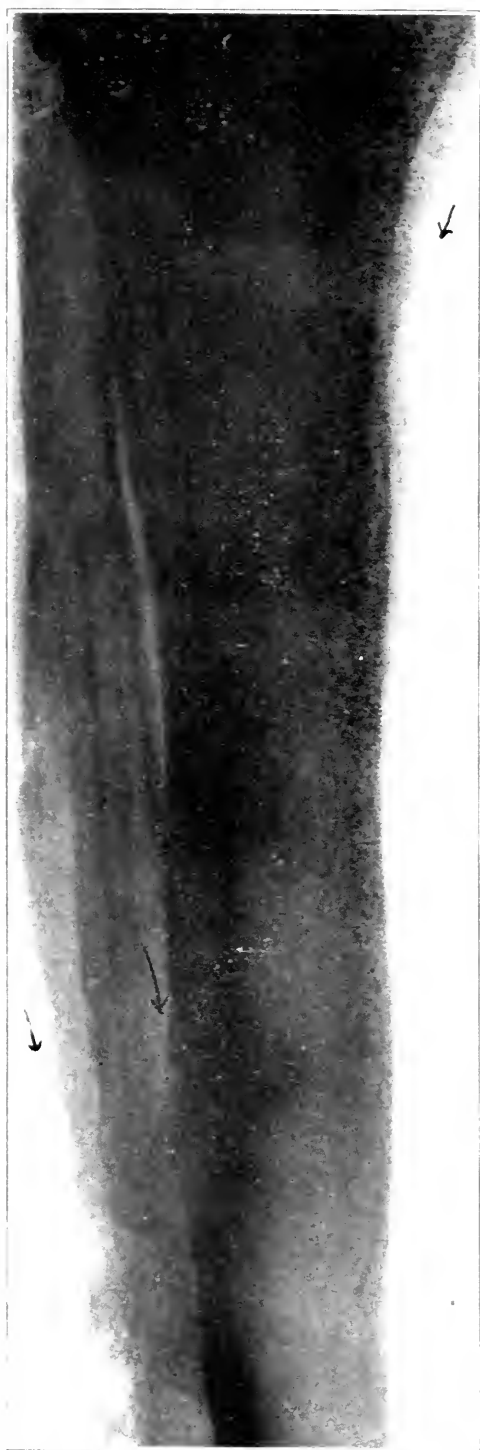


Fig. 6.—Specific osteoperiostitis tibia and fibula. Chronic ulcers of legs. Wassermann negative. No venereal history. Much improved for a time by specific treatment and ulcers healed, but later broke down. Male, age 56 years.





surgery, "There was in this group no bone syphilis, as the Wassermann reaction was done in each case, and all were negative."

In arriving at statistics of the number of syphilitics in a given community, too often these statistics are based on a serologic diagnosis alone. Groups of gynecologic, obstetric, and neurologic patients are examined by the hundreds in various clinics and the amount of syphilis in these groups is computed by the number of positive Wassermann reactions. In such statistics no account is taken of the number of cases which have syphilis and a negative reaction. Perhaps twenty per cent of old syphilitics have negative Wassermann reactions. If skeletal radiography were used in conjunction with serologic tests, and the findings passed upon by competent observers, the number of syphilitics in a given community would be very much augmented.

In surgical out-patient work, I have found that many obscure conditions have been cleared up by this method of diagnosis. Many of these cases have negative Wassermann reactions. In large hospitals and dispensaries, one is impressed with the number of cases that have been treated for years, in different clinical departments, always ailing with different troubles. We often find, through skeletal radiography, that an old syphilis is at the bottom of their troubles. The proof of the pudding is in the eating, and the almost magical way in which some of these cases are cured, or at least relieved of symptoms, by intensive specific treatment, is most striking. When skeletal manifestations of syphilis with symptoms are found through radiography, a most striking demonstration is completed by giving these patients specific treatment, and later taking other radiographs, which show definite changes for the better in the bone conditions.

Obscure swellings in the neck, supposed to be tuberculous glands, bursitis, and leg ulcerations, supposed to be varicose, have all had their correct etiology demonstrated by skeletal radiography. In such of these cases as I have had the opportunity to study, the Wassermann reaction has been oftener negative than positive. Skeletal radiography showing a specific bone picture in such cases gives presumptive evidence that the obscure trouble itself may be syphilis, and in a number of cases this has been proved by pathologic examination of tissue, and by the therapeutic test.

It is always wise to bear this point in view in cases of delayed or fibrous union of fractures and wounds that are ulcerated and take an inordinate time for healing.

In passing judgment in a suspected case, manifestly experience and long study are necessary, for there are numerous pitfalls into which the unwary may fall. Differences of bone structure which are normal must not be interpreted as pathologic and specific, and other abnormal bone conditions must be correctly differentiated. The workman will show a large and heavy tibia in the skiagraph, with a thick cortex, which is sometimes mistaken for a syphilitic periostitis. In viewing the two most often pictured bones, the tibia and the fibula, much care is necessary. The fibula, having many surfaces, is more difficult to judge by than the tibia, but periosteal proliferations on its surface, that are characteristic, are detected as often as on the tibia. The clavicle and bones of the forearm and hand will at times show lesions of silent syphilis, of the greatest value in diagnosis.

The use of skeletal radiography should be more common than it is at present, and its use in conjunction with the Wassermann reaction will give very accurate data as to the incidence of syphilis in different communities.

The accompanying radiographs illustrate some of the points touched upon in the preceding pages.

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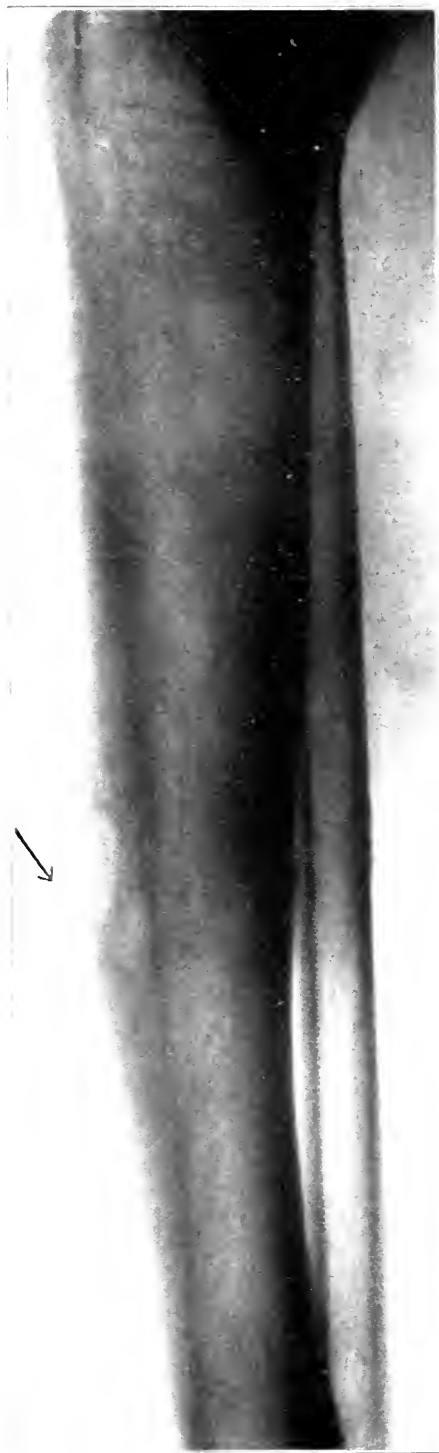


Fig. 7-A.



Fig. 7-B.

Fig. 7-A.—Female, age 53 years. Osteoperiostitis tibia. Gummatous infection. Acquired syphilis. Wassermann negative. No children, no miscarriages.

Fig. 7-B.—Female, age 53 years. Osteoperiostitis tibia. Gummatous infection. Acquired syphilis, five years' duration. Treatment at first. Wassermann negative.





Fig. 8.—Male. Specific osteoperiostitis tibia. Dilated aortic arch. No specific history.



Fig. 9.—Tibia. Girl, age 11 years. Specific periostitis. Fibrous union of fracture of clavicle until specific treatment was given.



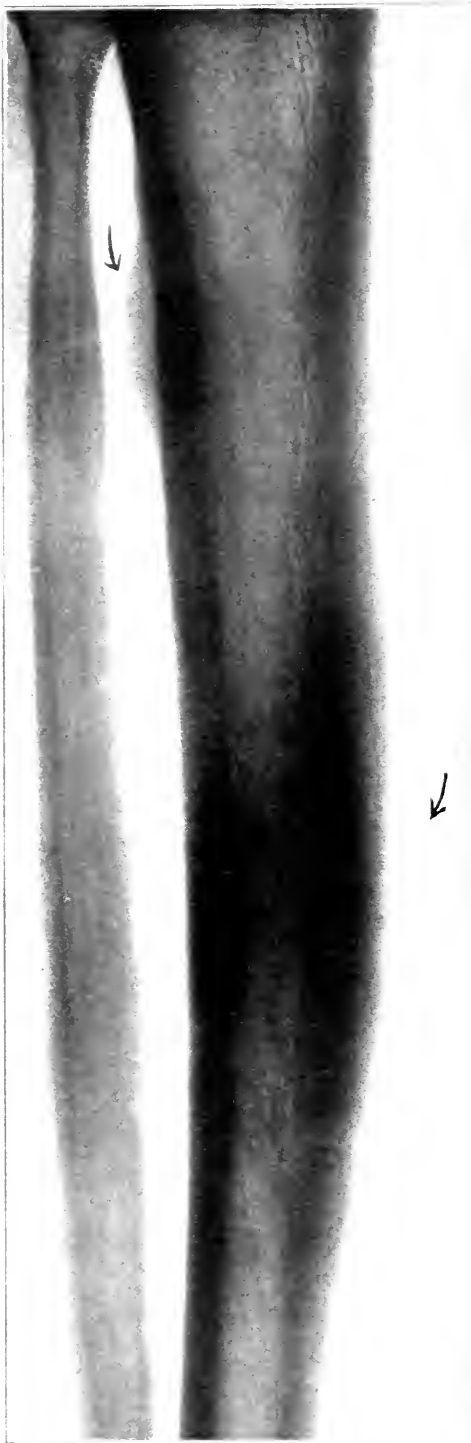


Fig. 10

Fig. 10.—Male, 45 years. Staphylococcal osteomyelitis of femur. Treatment of infection. No further evidence of active history of disease. Wassermann negative.



Fig. 11

Fig. 11.—Male, 4 years. Staphylococcal osteomyelitis of femur. Staphylococcal abscess. Wassermann negative. No further evidence of disease.







Fig. 12.

Fig. 12.—Male. Specific osteoperiostitis tibia and fibula. No specific history. Extensive injury to soft parts of leg. Healed by specific treatment.

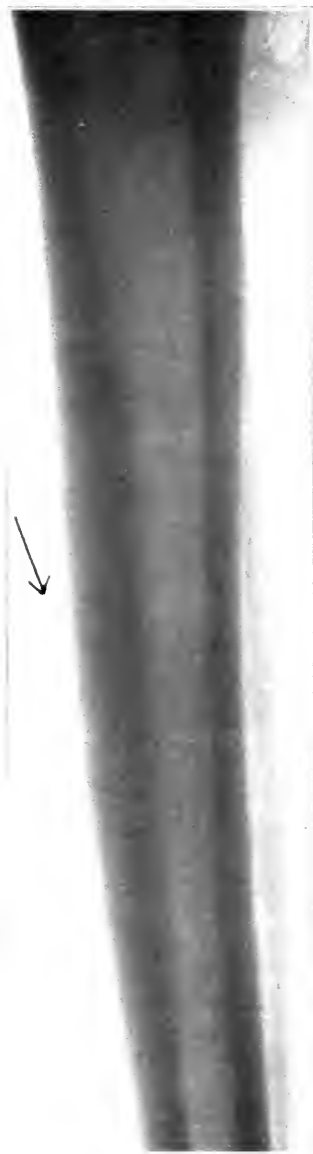


Fig. 13.

Fig. 13.—Female, 29 years. Specific osteoperiostitis tibia. Symptoms of angio spasm of right arm. Congenital.



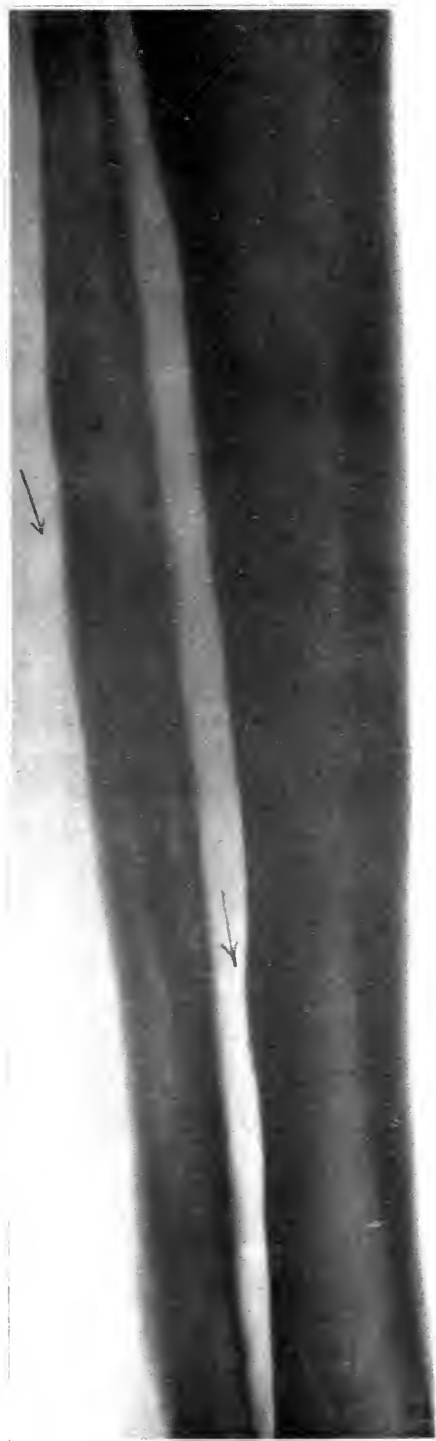


Fig. 14.—Male, 63 years. Specific osteoperiostitis tibia and fibula. Old specific history. Also had carcinoma of floor of mouth. Wassermann negative.



Fig. 15.—Male, 42 years. Specific periostitis tibia and fibula. History of syphilis at ten years. No ulcers of leg. Varying size veins. Ligation operation. Ulcers returned. Wassermann negative. Specific history obtained 4 years after operation. No incontinence, staggering gait, numbness of leg.



## THE BLOOD AND CEREBROSPINAL FLUID IN THREE HUNDRED KNOWN CASES OF SYPHILIS\*

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THIS paper is based upon the examination of the blood and cerebrospinal fluid in three hundred cases of syphilis; this series includes one hundred cases of early and two hundred cases of late syphilis. The four standard reactions were used: The Wassermann test on both the blood and cerebrospinal fluid (in a great number the alcoholic and cholesterin reinforced antigens were used), the cell count in the cerebrospinal fluid, the globulin test (Noguchi, which was the most successful in our hands), and Lange colloidal gold test. The Wassermann test is reported as negative, +, ++, +++, ++++. The findings in the cerebrospinal fluid are divided into four groups: negative, which is self-explanatory; slight changes, such as negative Wassermann on one-half cubic centimeter of fluid, cell count negative up to four, trace of globulin and slight change in the Lange's colloidal gold; moderate changes, such as Wassermann ++, cell count from four to eight, globulin + and a syphilitic curve in Lange's test; and marked changes such as Wassermann +++, cell count above eight, globulin ++ and +++, and marked curves in the Lange's colloidal gold reaction. The material is divided into two main parts—early syphilis and late syphilis. The early syphilis is divided into: primary, with or without adenopathy; early secondary, showing either a roseola or general papular eruption; and late secondary, characterized by condylomata lata, annular eruptions, etc. To this is added early treated syphilis, acute cerebrospinal meningitis, including those cases with a history of syphilis of eighteen

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\*Seventy-five of these cases were investigated by Dr. Dennie while on the staff of the Massachusetts General Hospital. He wishes to thank Dr. C. Morton Smith and Dr. J. Homer Wright for the privilege of studying these cases.

months or less, and all cases of syphilis without symptoms or marked signs less than eighteen months in duration. Late syphilis is divided into: gummata of the penis, phagedenic ulcers, untreated syphilis without symptoms, treated syphilis without symptoms, syphilis of the tongue, syphilis of the stomach, syphilis of the liver, syphilis of the bones and joints, syphilis of the skin, syphilis of the arteries, Raynaud's disease, congenital syphilis, optic atrophy, brain syphilis, old basilar meningitis, transverse myelitis, multiple sclerosis, progressive muscular atrophy, paresis, and tabes dorsalis.

## PRIMARY SYPHILIS

There were twenty cases in this group (Table I). The ones who gave entirely negative findings in the blood and cerebrospinal fluid were diagnosed primary syphilis because of the character of the lesion and the demonstration of the spirochete pallida by dark-field illumination. Six, or 30 per cent, had entirely negative blood and cerebrospinal fluid. Ten, or 50 per cent, had four plus positive serum reactions and entirely negative cerebrospinal fluid. Four, or 20 per cent, had four plus positive Wassermanns on the blood and mild findings in the cerebrospinal fluid. To make this more clear, 70 per cent

TABLE I  
PRIMARY SYPHILIS

NO.	B. WASS.	C. S. F. WASS.	C. C.	GLOB.	GOLD
1 EI.	neg.	neg.	neg.	neg.	0
2 R.	"	"	"	"	0
3 F.	"	"	"	"	0
4 JH.	"	"	"	"	0
5 S.	"	"	"	"	0
6 C.	"	"	"	"	0
7 HC.	++++	"	"	"	0
8 GR.	++++	"	"	"	0
9 MR.	++++	"	"	"	0
10 RA.	++++	"	"	"	0
11 GN.	++++	"	"	"	0
12 R.	++++	"	"	"	0
13 Hy.	++++	"	"	"	0
14 OB.	++++	"	"	"	0
15 FW.	++++	"	"	"	0
20 Smt.	++++	"	4	"	0
16 AF.	++++	"	4	tr.	0122100000
17 Pf.	++++	"	4	tr.	0122100000
18 Wt.	++++	"	neg.	tr.	1121000000
19 H.	++++	"	"	+	not done

had strong positive reactions on the blood, 80 per cent had entirely negative cerebrospinal fluids, 20 per cent had mild findings, and not one had marked findings in the cerebrospinal fluid.

## EARLY SECONDARY SYPHILIS

There were 40 cases in this group (Table II). Thirty-seven, or 92.5 per cent, had four plus positive Wassermanns on the blood; one was

TABLE II  
EARLY SECONDARY SYPHILIS

NO.	B. WASS.	C. S. F. WASS.	C. C.	GLOB.	GOLD
1 B.	++++	neg.	neg.	neg.	0
2 Bd.	++++	"	"	"	0
3 E.E.	++++	"	"	"	0
4 O.B.	++++	"	"	"	0
5 G.H.	++++	"	"	"	0
6 Gy.	++++	"	"	"	not done
7 B.R.	++++	"	"	"	0
8 L.C.	++++	"	"	"	0
9 T.	++++	"	"	"	0
10 B.	++++	"	"	"	0
11 S.	++++	"	"	"	0
12 G.	++++	"	"	"	0
13 K.	++++	"	"	"	0
14 B.H.	++++	"	4	"	0
15 E.M.	++++	"	1	"	0
16 J.H.	++++	"	neg.	tr.	not done
17 E.M.	++++	"	3	neg.	not done
18 Sm.	++++	"	4	tr.	1111000000
19 Str.	++++	"	neg.	neg.	0011000000
20 CP.	++++	"	2	"	0011000000
21 D.F.	++++	"	4	+	1123321000
22 Br.	++++	"	neg.	tr.	1234432100
23 J.W.	++++	"	4	tr.	1121000000
24 S p.s.	++++	"	7	tr.	not done
25 Grf.	++++	"	neg.	tr.	1122100000
26 Lng.	++++	"	"	tr.	1110000000
27 Bogd.	++++	"	"	not done	0012210000
36 Lvly.	neg.	"	9	+++	not done
37 Ashly.	"	"	neg.	neg.	not done
38 W.A.	++++	"	12	tr.	0012210000
39 M.F.		"	6	+	negative
40 Mels.	++++	"	8	neg.	negative
28 Brsm.	++++	++	neg.	tr.	1234432110
29 Spgl.	++++	++ 1 c.c.	35	+	not done
30 Wrng.	++++	++ 1 c.c.	2	+	0123321000
31 Sc.	++++	++ 1 c.c.	8	neg.	not done
32 Gbsn.	++++	+++	neg.	tr.	0012210000
33 Krwn.	++++	+++	10	tr.	0012110000
34 Copr.	++++	++++	neg.	++	0123210000
35 Grnbg.	++++	++++ 2 c.c.		+	1122100000

not done and two were under salvarsan treatment at the time. Eight, or 20 per cent, gave positive Wassermanns on the cerebrospinal fluid, but it will be noted that one-half of these gave two plus and, furthermore, in four one cubic centimeter or more of cerebrospinal fluid was used. Eighteen, or 45 per cent, gave entirely negative cerebrospinal fluids. Fourteen, or 35 per cent, had mild findings, and 8, or 20 per cent, had marked findings in the cerebrospinal fluid.

## LATE SECONDARY SYPHILIS

In this classification (Table III) the diagnosis of late secondary syphilis was both upon the duration of the disease (less than two years) and upon the clinical manifestations. Over 85 per cent had condylomata lata about the rectum or genitals, which were very

TABLE III  
LATE SECONDARY SYPHILIS

NO.	B. WASS.	C. S. F. WASS.	C. C.	GLOB.	GOLD
1 Dzntg.	++++	neg.	neg.	neg.	0
2 Mnklr.	++++	"	9	tr.	1234321000
3 Dvs.	++++	"	10	tr.	0011232100
4 Prkr.	++++	"	neg.	tr.	not done
5 Dks.	++++	"	4	neg.	0
6 Smh.	++++	"	4	tr.	1110000000
7 Hmltn.	++++	"	11	++	0013200000
8	++++	"	4	+	
9 Fld.	++++	"	4	+	1123321000
10 Gry.	++++	"	8	tr.	0012200000
11 Andr.	++++	"	12	tr.	1122100000
30 Les.	++++	"	9	+	0011100000
12 Crglr.	++++	+++	20	+	0012221000
13 Lamn.	++++	++++	66	+++	4555543200
14 Hrs.	++++	++++	40	+	not done
15 Klr.	++++	++++	8	+	not done
16 Brn.	++++	++++	20	+	not done
17 Smth.	++++	++++ 2 c.c.	neg.	tr.	1122110000
18 Lg.	++++	++++	"	tr.	1122100000
19 Wpl.	++++	++++	2		1233210000
20 A. Andr.	++++	++++	10	++	1123320000
21 Rdubg.	++++	++++	4	tr.	1122100000
22 Hrngtn.	++++	++++	4	++	1122100000
23 Wctr.	++++	++++	8	++	1123321000
24 Yng.	++++	++++	neg.	+	0112210000
25 Rds.	++++	++++		not done	
26	++++	++++	neg.	++	1233220000
27 Brsngtn.	++++	++++		not done	
28 St. M.	++++	++++	40	+++	0123321000
29 T. E.	++++	++++	200	+++	1133100000
31 Mc. Crd.	++++	+++	130	++	1213310000



active at the time, the remainder had either recurrent roseolas or late secondary papular eruptions somewhere on the body.

One hundred per cent gave four plus positive Wassermanns on the blood, and 60 per cent upon the cerebrospinal fluid. Two, or 7 per cent, had entirely negative findings in the fluid. Nine, or 33 per cent, had moderate findings in the fluid. In other words, 60 per cent gave undoubted evidence of meningeal involvement and 33 per cent more gave some evidence of such involvement. The clinical evidence to a large extent was in accordance with these findings. A large number of these patients complained of frequent headaches, the pupils were dilated, and reacted to light but somewhat tardily. The knee-jerks were plus. Ear examination of a few by Dr. S. E. Roberts revealed undoubted evidence of eighth nerve involvement. One case, No. 8, had unequal pupils.

The reason that these cases of late secondary syphilis show more meningeal involvement than primary and early secondary syphilis is twofold: First, the disease is of longer duration; and second, but most important, the character of the skin manifestation is the determining factor. It is a well-known fact that condylomata lata are the most infectious of all acquired lesions. In a former paper\* attention was drawn to the fact that *treponemata pallidæ* were not only present in these lesions but that they rapidly multiplied in the lymph spaces between the prickle cells, and migrated, not only toward the surface, but in the deeper lymph spaces as well, thus gaining entrance to the blood stream. Therefore these condylomata act as incubators for the production of enormous numbers of these organisms. It follows as a natural conclusion that the meninges are being subjected to a continual bombardment and must finally allow the passage of these organisms.

## TREATED SYPHILIS (EARLY)

TABLE IV

## TREATED SYPHILIS (EARLY)

NO.	B. WASS.	C. S. F. WASS.	C. C.	GLOB.	GOLD
1 J.P.L.	neg.	neg.	neg.	neg.	neg.
2 S.S.	"	"	"	"	"
3 M.A.	"	"	"	"	"
4 Wklr. iritis	+++	"	9	tr.	1234320000
5 C.E.	+++	+++	30	++	0123200000
6 Ynr.	neg.	+++	130	++	1124321000

\*Jour. Cutan. Dis., July, 1914.

This group (Table IV) represents cases of less than eighteen months' duration, all of whom had from one to eight intravenous injections of salvarsan and from ten to eighty intramuscular injections of metallic mercury or its insoluble salts. Nos. 1, 2, 3, and 5 did not complain of any symptoms nor did they show any signs of syphilis. No. 4 had an acute iritis, and No. 6 an epileptiform attack, preceded by headaches and buzzing of the left ear, evidently a basilar meningitis. The first three were entirely negative in all respects, the last three gave abundant evidence of meningeal involvement. Nos. 5 and 6 had received the most vigorous treatment of all. Even this small number of treated patients demonstrates the fact that the cerebrospinal fluid of every person with early syphilis should be investigated.

#### CEREBROSPINAL MENINGITIS (ACUTE, SYPHILITIC)

All five cases (Table V) had headaches, dizziness, and nausea. All had exaggerated knee-jerks and dilated pupils. All had strongly positive serum reactions and marked findings in the cerebrospinal fluid. It will be noted that all but one had the so-called parietic curve, in fact all the findings were identical with those of acute paresis.

TABLE V

#### CEREBROSPINAL MENINGITIS (ACUTE, SYPHILITIC)

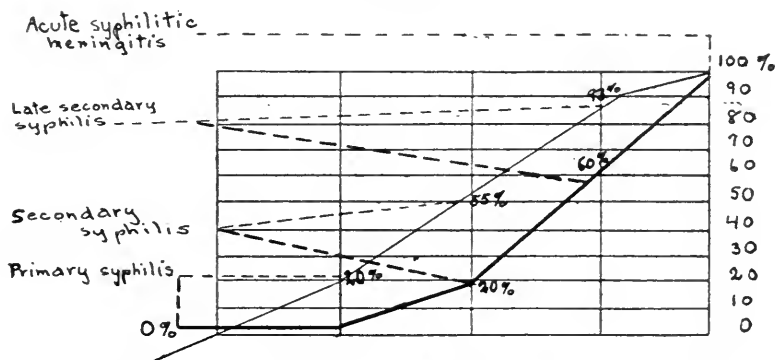
NO.	B. WASS.	C. S. F. WASS.	C. C.	GLOB.	GOLD
1 A.C.	++++	++++	612	+++	5555543210
2 G.	++++	++++	606	+++	5555432100
3 B.	++++	++++	2400	+++	5555543210
4 GLD.	++++	++++	1200	+++	5554221000
5 E.D.	++++	++++	560	+++	0012345543

This is probably due to the fact that these patients not only had a meningitis but an involvement of the deeper structures of the brain and cord as well. These findings are simply an indication of an active, extensive involvement of the entire development of the brain and spinal cord. The curve in gold solution, number five, is that of a septic meningitis and can not be accounted for, as the patient is still living. Two interesting facts were noted in this group: First, patients with an extremely high cell count had 20 or more per cent of polymorphonuclear leucocytes, which is against the rule in syphilis; and secondly, insufficient treatment with salvarsan alone seems to

predispose them to meningeal involvement, as all of these patients had from one to four intravenous doses of salvarsan early in the disease without any subsequent treatment. All developed this condition within six months after the last dose.

In reviewing these cases of early syphilis, a graphic chart is shown (Table VI); the heavy black line indicating the undoubted per cent of meningeal involvement as evinced by marked and moderate findings in the cerebrospinal fluid and the lighter line indicating in addition the mild findings. We believe with Fordyce and others that slight findings in the cerebrospinal fluid are not evidence of involvement of the central nervous system but an indication of meningeal irritation due to a general infection.

TABLE VI



Percentage of undoubted meningeal involvement in all cases of early syphilis—60%.

Percentage that show changes of all kinds from mild to marked in all cases of early syphilis—67%.

## GUMMATA OF PENIS

TABLE VII

## GUMMATA OF PENIS

NO.	B. WASS.	C. S. F. WASS.	C. C.	GLOB.	GOLD
1 Gun.	+++	++ 1 c.c.	10	++	1233210000
2 Lvr.	+++	neg.	neg.	tr.	0012100000
3 Gunn.	+++	"	"	++	0012100000
4 Cus.	+++	"	7	+	0011100000
5 Pt.	++	"	4	tr.	0122100000
6 Mrt.	neg.	"	4	+	1123100000

Gummata of the penis (Table VII) are not rare, and are usually diagnosed as chancroids. In nearly all instances they are due to syphilitic endarteritis of some of the smaller vessels. In five of these cases the blood was positive, the cerebrospinal fluid of all showed evidence of syphilis, although the findings were mild.

## PHAGEDENIC ULCERS

Phagedenic ulcers (Table VIII) will be considered from an entirely different angle than that usually presented. From a study of these four cases the conclusion was drawn that these manifestations were more likely to occur in patients suffering from old syphilis.

TABLE VIII  
PHAGEDENIC ULCERS

NO.	B. WASS.	C. S. F. WASS.	C. C.	GLOB.	GOLD
1 Calhn.	+++	neg.	neg.	neg.	negative
2 Colmn.	+++	"	"	"	0122100000
3 Smth.	neg.	+++	3	+	0122310000
4 Strtr.	neg.	neg.	7	++	0123210000

In three of these cases an undoubted history of syphilis of several years' standing was obtained. Case No. 3 denied an infection of any kind; while his blood was negative, his cerebrospinal fluid was markedly positive; a radiograph of his tibiæ revealed a marked thickening of the cortices, such as is often observed in the congenital type. Case 2 went to autopsy, a pathologic examination of the tissue showed typical syphilitic endarteritis of the penial artery near its origin. These findings, together with undoubted serologic evidence of syphilis in all the cases, make one draw the conclusion that phagedenic ulcers are due to a syphilitic endarteritis with coincident infection (it makes no difference what) of the devitalized tissues.

## UNTREATED SYPHILIS (OLD) WITHOUT SYMPTOMS

This series of cases (Table IX) was thrown into two groups. First, those who had received no treatment during the last five years and before that time treated indifferently; and secondly, those who, in the course of routine examination, gave positive Wassermanns. Nearly all gave a history of syphilis, and in the greater number

TABLE IX  
UNTREATED SYPHILIS (OLD) WITHOUT SYMPTOMS

NO.	B. WASS.	C. S. F. WASS.	C. C.	GLOB.	GOLD
1 Frl.	neg.	neg.	neg.	neg.	neg.
2 Luch.	"	"	"	"	"
3 Lfd.	"	"	"	"	"
4 T.G.H.	"	"	"	"	"
5 Cly.	"	"	14	"	"
6 P.J.	"	"	neg.	tr.	syphilis
7 Lfr.	not done	"	"	+++	"
8 Mc.C.	neg.	"	"	+++	"
9 Unh.	+++ .5 c.c.	"	"	neg.	neg.
10 S.M.	++	"	"	"	"
11 T.H.	++++	"	"	"	"
12 T.C.	++++	"	"	"	"
13 R.J.	++++	"	"	"	"
14 L.J.E.	++++	"	1	"	"
15 W.F.	++++	"	8	tr.	syphilis
16 P.J.	++++ 1 c.c.	"	4	+	"
17 Lnds.	++++	"	neg.	++	"

signs of past syphilis were in evidence. Eight, or nearly 50 per cent, gave negative blood findings, but of this number 3 gave evidence of syphilis in the cerebrospinal fluid. The remaining 9 gave positive blood Wassermanns, and of this number 3 gave evidence of syphilis in the cerebrospinal fluid. It is of the utmost importance in these old cases of syphilis to make a complete examination of the cerebrospinal fluid as one-third of them at least will show confirmatory evidence from that source.

TREATED SYPHILIS (OLD) WITHOUT SYMPTOMS

TABLE X  
TREATED SYPHILIS (OLD) WITHOUT SYMPTOMS

NO.	B. WASS.	C. S. F. WASS.	C. C.	GLOB.	GOLD
1 S.M.	neg.	neg.	neg.	neg.	neg.
2 G.F.	"	"	"	"	"
3 S.O.	"	"	"	"	"
4 H.W.	"	"	"	"	"
5 A.A.	"	"	1	"	"
6 McK.	"	"	neg.	"	syphilis
7 E.C.K.	"	++ .75 c.c.	"	tr.	neg.
8 L.G.	"	++++ 1 c.c.	"	"	syphilis
9 C.M.B.	++++	neg.	"	"	neg.
10 M.K.	++++	"	"	"	"
11 A.E.	++++	"	"	"	"
12 C.R.	++++	"	"	"	"
13 B.R.	++++	"	"	"	"
14 C.A.	++++	"	"	"	"

This series (Table X) represents cases of old syphilis who had received energetic treatment over some period of time. Six retained positive four plus Wassermanns; of these three gave confirmatory evidence in the cerebrospinal fluid. Eight had negative blood Wassermanns, and of these three gave evidence of syphilis in the cerebrospinal fluid. There was not much difference between the treated and untreated cases of old syphilis so far as the serology was concerned.

TABLE XI

NO.	B. WASS.	C. S. F. WASS.	C. C.	GLOB.	GOLD
SYPHILIS OF THE TONGUE					
1 Mc.P.	+++	neg.	neg.	neg.	neg.
2 F.J.	+++	"	"	"	"
Both had positive blood and entirely negative fluids.					
SYPHILIS OF THE STOMACH					
1 G.H.	+++	neg.	neg.	neg.	neg.
2 K.H.	+++	"	"	"	"
Both had positive blood and negative cerebrospinal fluids.					
SYPHILIS OF THE LIVER					
1 K.	+++	neg.	neg.	neg.	neg.

This last case had positive blood and negative cerebrospinal fluid. It is admitted that there are not enough cases of visceral syphilis upon which a conclusion could be drawn, but it is interesting to note that the cerebrospinal fluids of all three were negative. (Table XI.)

TABLE XII

## SYPHILIS OF THE BONES AND JOINTS

NO.	B. WASS.	C. S. F. WASS.	C. C.	GLOB.	GOLD
1 G.R.	neg.	neg.	neg.	neg.	neg.
2 L.F.	"	"	"	"	"
3 S.G.	"	"	"	"	"
4 Crk.	"	++	"	tr.	syphilis
5 Y.H.	+++	neg.	neg.	neg.	neg.
6 L.M.	+++	"	"	"	"
7 F.J.	+++	"	"	"	"
8 Pst.	+++	"	"	"	0011000000
9 N.C.	+++	"	"	"	syphilis
10 Tek.	+++	"	9	+	"
11 J.J.	+++	"	14	tr.	"
12 Mc.C.	+++	+++ 1 c.c.		+	"

These cases (Table XII) include syphilitic arthritis, necrosis of the bones of the face and skull, and syphilitic changes in the long bones. Sixty-six and two-thirds per cent gave strongly positive Wassermanns on the blood. Twenty-five per cent gave negative findings on both the blood and cerebrospinal fluid. Forty per cent gave confirmatory evidence of syphilis in the cerebrospinal fluid.

TABLE XIII  
SYPHILIS OF THE SKIN

NO.	B. WASS.	C. S. F. WASS.	C. C.	GLOB.	GOLD
1 P.A.	neg.	neg.	neg.	neg.	neg.
2 Prv.	++++	“	“	11	syphilis
3 Ostr.	++++	“	“	neg.	neg.
4 Crz.	++++	“	6	“	“
5 K.R.	++++	“	8	+	“
6 S.A.G.	++++	++	20	+++	syphilis
7 O.J.	++++ .3	++++ 1	neg.	+	“
8 Brd.	++++	++++ 1	4	+	“
9 Wls.	++++	++++	70	+	not done
10 P.E.	++++	++++	75	+++	syphilis

These were all cases of old syphilis of the skin without symptoms of central nervous system involvement (Table XIII). All but one gave strongly positive Wassermanns on the blood. Fifty per cent gave marked findings in the cerebrospinal fluid, and 20 per cent more gave mild reactions. Patients with old syphilis of the skin are more likely to show positive cerebrospinal fluids than any other type of old syphilis excepting, of course, clear cut syphilis of the central nervous system. The percentage of positive blood is also higher in this type than any other type of old syphilis excepting only paresis.

TABLE XIV  
RAYNAUD'S DISEASE

NO.	B. WASS.	C. S. F. WASS.	C. C.	GLOB.	GOLD
1 S.	++++	neg.	neg.	neg.	neg.
2 B.	++++	++	10	tr.	syphilis

Both cases in Table XIV had strongly positive blood Wassermanns and one showed moderate evidences in the cerebrospinal fluid. Raynaud's disease should always be investigated for syphilis.

TABLE XV  
SYPHILIS OF THE ARTERIES

NO.	B. WASS.	C. S. F. WASS.	C. C.	GLOB.	GOLD
1 D.C.	++++	++++	63	+	syphilis
2 Hnz.	++++	++++	neg.	+	"
3 Bhn.	++++	++	10	neg.	neg.
4 Stn.	++++ 3	neg.	neg.	+++	"

One hundred per cent gave positive serologic findings on both the blood and cerebrospinal fluid. In cases of arterial disease, spinal fluid should always be examined.

CONGENITAL SYPHILIS

1 Lan.	++++	++++	10	+	syphilis
2 M.	++++	++	neg.	tr.	"
3 M2.	++	++	"	tr.	"
4 Mrfy.	++++	neg.	"	neg.	neg.
5 M.	++++	"	"	"	"
6	++++	"	"	"	"
7	++++	"	"	"	"
8	++++	"	"	"	"
9	++	"	"	"	"

One hundred per cent of these cases (Table XV) had positive blood Wassermanns and only thirty per cent gave evidence of syphilis in the cerebrospinal fluid examination. The larger percentage of these cases were children with joint or bone conditions. Two had family ataxia and the rest had either Hutchinson's teeth, interstitial keratitis, or some other stigmata of congenital syphilis.

TABLE XVI  
OPTIC ATROPHY

NO.	B. WASS.	C. S. F. WASS.	C. C.	GLOB.	GOLD
1 Dvs.	++++	++++	neg.	+	syphilis
2 T.A.	++++	++++	"	+	not done
3 B.R.	neg.	++++	"	+	0011000000
4 Blk.	not done	++	7	+	syphilis

These cases of optic atrophy (Table XVI) had all received energetic treatment after the process had started, but before spinal puncture had been done, all had markedly positive fluids, showing that there was an accompanying meningeal involvement.

In this group (Table XVII) were placed those cases of brain syphilis of the vascular type, who had shown transitory palsies, sensory paralysis, or apoplexy, and those cases who gave evidence



TABLE XVII  
BRAIN SYPHILIS

NO.	B. WASS.	C. S. F. WASS.	C. C.	GLOB.	GOLD
1 J.S.	not done	neg.	3	+	syphilis
2 Mr. B.	neg.	"	10	+	"
3 Mrs. B.	"	"	9	+	"
4 Mns.	"	++++ 2 c.c.	neg.	tr.	"
5 Hst.	"	++++ 1 c.c.	4	+	"
6 I.E.	not done	+	6	+	"
7 Ste.	++++	neg.	4	++	"
8 M.P.	++++	"	10	++	not done
9 Wls.		"	4	neg.	syphilis
10 P.J.	++++	"	neg.	"	"
11 Gml.	++++	"	25	"	not done
12 Etk.	++++	"	neg.	tr.	syphilis
13 C.B.	not done	"	5	tr.	"
14 Tur.	++++	++++	6	++	"
15 Gsy.	++++	+++	100	+++	"
16 W.J.	++++	++++	3	++	neg.
17 R.F.D.	++++	++++	20	++	syphilis
18 P.C.	++++	++++	4	++	"
19 O.J.	++++	++++	6	neg.	neg.
20 M.W.A.	++++	++++	93	+	syphilis
21 B.A.		++++	65	++	"
22 S.J.		++++	5	neg.	neg.
23 Sft.		++++	10	tr.	"
24 Mc.C.		++++	8	+	"

of basilar meningitis, such as headaches, dizziness, and ringing in the ears with irregular unequal pupils and exaggerated reflexes. With a few exceptions the findings in the cerebrospinal fluid of this type of cases are not as marked as in the earlier cases of brain syphilis. This is especially true in the vascular type of which the first five are good examples. Over 50 per cent of these cases gave negative Wassermanns on the cerebrospinal fluid unless more than 1 c.c. was used, while 80 per cent gave positive globulin and 90 per cent gave positive Lange's reactions. Forty-five per cent gave marked findings in the cerebrospinal fluid. In this last group the clinical symptoms were very marked, and were definitely those of basilar meningitis.

Headaches were the only symptom in this group of cases. There were apparently no signs of central nervous system involvement. Seven, or 64 per cent, had marked findings in the cerebrospinal fluid. Three, or 28 per cent, had mild reactions and one was negative. The blood was positive in all but two cases and these gave evidence

TABLE XVIII  
CEREBROSPINAL MENINGITIS (OLD)

NO.	B. WASS.	C. S. F. WASS.	C. C.	GLOB.	GOLD
1 P.Ftn.	++++	++++	148	+++	1234332100
2 P.Dvrs.	++++	++++	15	++	0011000000
3 C.Novl.	++++	++++	88	++	0012321000
4 H.Ntn.	++++	++++	10	+	0012210000
5 G.Nkls.	++++	++	7	+	0012321000
6 B.Gln.	+	++	28	++	0011000000
7 J.Lns.	++++	neg.	38	++	0003554130
8 Syr.	++++	“	neg.	neg.	0012210000
9 G.Nkls.	++	“	“	“	0
10 E.Av.	neg.	++++	19		
11 T.Shrn.	“	neg.	5	+++	

of syphilis in the cerebrospinal fluid. Headaches without other symptoms or signs is a significant factor in those who have syphilis.

TABLE XIX  
PARESIS

NO.	B. WASS.	C. S. F. WASS.	C. C.	GLOB.	GOLD
1 J.H.W.	++++	++++	26	+++	55555555453
2 D.G.F.	++++	++++	100	+++	55555553011
3 Mc.Co.	++++	++++	30	+++	5555555533
4 S.T.	++++	++++	92	+++	55555434211
5 Rdg.	++++	++++	725	+++	5555555542
6 Sch.	++++	++++	76	+++	5555555421
7 Man.	++++	++++	240	+++	5555555431
8 A.E.	++++	++++	66	+++	55455555210
9 N.W.L.	++++	++++	280	+++	455555545310
10 S.D.	++++	++++	75	+++	44455323000
11 Mc.G.	++++	++++	38	+++	2223443210
12 Mst.	not done	++++	32	+++	0001122454

In paresis the blood and cerebrospinal fluid, almost without exception, gave marked positive evidence of syphilis. Eighty per cent gave the so-called paretic curve; in two cases, eleven and twelve, the Lange's reaction was not that usually found; one gave the tabetic curve and the other that of septic meningitis.

Tabes dorsalis (Table XXI) was divided into five classes:

1. Those who gave marked findings in both the blood and cerebrospinal fluid. Forty-six, or 70 per cent, belonged to this group. This class represents the type of tabes which is very active.

2. Those who had positive blood and mild findings in the cerebro-

TABLE XX

NO.	B. WASS.	C. S. F. WASS.	C. C.	GLOB.	GOLD
TRANSVERSE MYELITIS					
1 K.M.P.	neg.	++++	15	++++	55555555453
In this case the entire findings were strongly positive and the Lange's test was the so-called paretic curve.					
MULTIPLE SCLEROSIS					
1 K.P.	++++	++++	50	++	syphilis
In this case the findings were all strongly positive.					
PROGRESSIVE MUSCULAR ATROPHY					
1 B.A.	neg.	neg.	20	++	syphilis
This case gave some evidence of syphilis in the cerebrospinal fluid.					

spinal fluid. Five, or 8 per cent, belonged to this group. This is interpreted to mean that the syphilitic process is almost at a standstill in the central nervous system, but is still active elsewhere.

3. Those who had positive blood but negative cerebrospinal fluid. There were three cases, or 5 per cent, in this group. In this class the syphilitic process was at a standstill in the central nervous system but active elsewhere.

4. Those who had negative blood but positive cerebrospinal fluids.

TABLE XXI  
TABES DORSALIS

NO.	B. WASS.	C. S. F. WASS.	C. C.	GLOB.	GOLD
1 P.J.	++++	++++	100	+	syphilis
2 H.J.	++++	++++	28	++	"
3 Mc.G.	++++	++++	80	not done	"
4 C.C.	++++	++++	65	++	"
5 Mc.C.	++++	++++	110	+++	"
6 R.M.	++++	++++	40	++	"
7 G.S.	++++	++++	30	+	"
8 C.M.J.	++++	++++	18	++	"
9 D.C.	++++	++++	63	+	"
10 D.C.	++++	++++	34	++	"
11 P.G.	++++	++++	89	+++	"
12 C.J.	++++	++++	29	++	"
13 F.C.	++++	++++	8	++	"
14 R.L.	++++	++++	18	+	"
15 D.G.	++++	++++	35	+	"
16 A.H.	++++	++++	136	+	"
17 Mc.C.	++++	++++	45	++	"
18 Ltn.	++++	++++	55	+++	"
19 Cls.	++++	++++	20	++	"
20 Cgn.	++++	++++		+++	"

TABLE XXI (CONTINUED)

## TABES DORSALIS

NO.	B. WASS.	C. S. F. WASS.	C. C.	GLOB.	GOLD
21 Msg.	++++	++++	60	+++	"
22 S.A.	++++	++++	10	+++	"
23 N.M.N.	++++	++++	120	+++	"
24 N.J.	++++	++++	14	+++	"
25 H.J.	++++	++++	70	+++	"
26 F.G.N.	++++	++++	38	+	"
27 B.J.	++++	++++	40	++	"
28 Cml.	++++ .2	++++ 1 c.c.	20	+	"
29 Hgt.	++++	++++ 1 c.c.	50	+	"
30 Hky.	++++ .3	++++ 1 c.c.	20	+	not done
31 Knd.	++++	++++ 1 c.c.	20	++	syphilis
32 Ltz.	++++	++++ 1 c.c.	2	tr.	"
33 Lgn.	++++	+++	0	+	"
34 Frs.	+++	++++ 1 c.c.	10	tr.	"
35 Mc.C.	++++	++++ 2 c.c.	32	++	"
36 J.R.	++++	++++		not done	
37 D.E.C.	++++		63	++	"
38 B.L.		++++	42	+	"
39 V.P.		++++	56	++	"
40 T.R.	++++		21	+	"
41 H.A.	++	++++	7	neg.	"
42 R.A.	++	++++	101	++	"
43 Mc.D.	++	++++	14	++	"
44 Bhr.		++++	120	++	"
45 C.E.	++++	++	15	++	"
46 S.J.	++	++	6	tr.	"
47 D.A.	++++	neg.	85	++	"
48 S.M.J.	++++		21	++	
49 Gnz.	++++	"	0	tr.	"
50 Lhl.	++++	"	0	++	
51 P.M.	++		10	+	
52 Mc.I.	neg.	++++	6	++	syphilis
53 S.M.	"	++++	84	++	"
54 Bly.	"	++++	19	++	"
55 M.M.	"	+	8	0	"
56 Mat.		neg.		+++	"
57 M.S.	"	"	28	++	"
58 Drn.	++++	"	0	0	neg.
59 Win.	++++	"	0	0	"
60 Rs.	++++	"	0	0	"
61 D.J.	++++	++++	74	+++	5555553410
62 B.P.S.	++++	++++	145	++	54555534200
63 J.M.P.	++++	++++	85	+++	4454545421000
64 De.G.	++++	neg.	27	++	454545453431000

There were six cases, or 9 per cent, in this group. This, of course, meant that the process was active as shown by cerebrospinal fluid but less so elsewhere.

5. Those who had positive blood and positive cerebrospinal fluids

with the so-called paretic curve with Lange's test. These cases were not taboparesis, but represented a very active type of tabes.

#### GENERAL DISCUSSION

There has been some question regarding the origin of the syphilitic antibody in the cerebrospinal fluid. It is held by some that these antibodies pass through the meninges from the blood stream, others claim that the central nervous system itself forms these bodies when it is attacked by syphilis. Both views are probably correct. In old cases of syphilis with strongly positive Wassermanns on the blood and no symptoms or signs of central nervous system involvement, positive Wassermanns can be secured on the cerebrospinal fluid if 1 c.c. or more are used. Bohan has called attention to this phenomenon. This can be accounted for by the fact that the patient has carried a positive blood Wassermann for years and during this time there has been a slow filtration of syphilitic amboceptor through the meninges. But in cases of syphilitic disease of the central nervous system an altogether different condition exists. Where the disease is active, a strongly positive Wassermann is always secured with small amounts of cerebrospinal fluid, when the blood Wassermann may be negative even if large amounts of serum are used, this would seem to indicate that the central nervous system itself was a factor in the production of syphilitic antibodies.

The examination of the cerebrospinal fluid of syphilitics with central nervous system involvement gives a clear idea of the activity of the disease. When all the findings are strongly positive, the disease is very active and also very extensive. The cell count alone is an index to the activity of the disease. Thus a patient with a positive four plus Wassermann on the blood and cerebrospinal fluid (small amounts being used), a cell count of three hundred, the so-called paretic curve with Lange's test, and marked globulin is not necessarily a paretic. These findings are simply an indication of the activity of the disease and the patient may have either cerebrospinal meningitis (syphilitic), tabes, transverse myelitis, late secondary syphilis with meningeal involvement, or paresis. Cases of central nervous system syphilis of long standing will often show very indefinite findings in the cerebrospinal fluid. A typical example is one with a negative spinal fluid Wassermann, a negative cell count,

one plus globulin, and a syphilitic curve in the gold solution. This simply means that the activity of the disease is almost at a standstill. There are all variations between these two classes.

It will be noted that a great number of the old cases of syphilis without apparent disease of the central nervous system will show positive globulins, a syphilitic curve with Lange's test and a negative cell count and a negative Wassermann reaction unless large amounts of fluid are used. We do not believe that these findings are indicative of central nervous system involvement, but are to be interpreted as confirmatory evidence of syphilis.

#### CONCLUSIONS

1. In primary syphilis, the cerebrospinal fluid was entirely negative in 80 per cent of the cases and of the remaining 20 per cent the findings were very mild.

2. In secondary syphilis, the cerebrospinal fluid was entirely negative in 45 per cent; 35 per cent had mild reactions, and 20 per cent marked findings.

3. In late secondary syphilis, the blood Wassermans were 100 per cent positive; 60 per cent gave undoubted evidence of meningeal involvement as the cerebrospinal fluid in these cases was markedly positive throughout; 33 per cent had moderate findings in the cerebrospinal fluids; and only 7 per cent had entirely negative cerebrospinal fluids.

4. Early treated syphilis should have an examination of the cerebrospinal fluid before the treatment is finished, as 50 per cent of the series reported here had positive findings in the cerebrospinal fluid without signs or symptoms of central nervous system involvement.

5. Cerebrospinal meningitis (syphilitic, acute) had the same findings in the cerebrospinal fluid, even to the paretic curve with the gold solution as paresis.

6. Gummata of the penis did not have marked findings in the cerebrospinal fluid, but the confirmatory type.

7. The phagedenic ulcers reported here were evidently due to late syphilis.

8. Old syphilis without symptoms, treated and untreated, have almost the same findings in the blood and cerebrospinal fluid. One-

third show confirmatory evidence of syphilis in the cerebrospinal fluid.

9. Syphilis of the tongue, stomach, and liver did not show any evidence of syphilis in the cerebrospinal fluid.

10. The larger percentage of syphilis of the bones and joints shows confirmatory evidence of lues in the cerebrospinal fluid.

11. Fifty per cent of the cases with syphilis of the skin (old) showed marked evidence of syphilis in the cerebrospinal fluid. This report is decidedly against the old teaching.

12. Raynaud's disease should always be investigated for old syphilis.

13. Congenital syphilis did not show many positive cerebrospinal fluids.

14. Syphilis of the arteries (aortitis, aneurysm) all showed positive cerebrospinal fluids.

15. Patients with optic atrophy all had positive cerebrospinal fluids (evidence of a meningeal involvement).

16. Brain syphilis of the vascular type had mild findings in the cerebrospinal fluid. The chronic basilar meningitic type had marked findings in the cerebrospinal fluid.

17. In cerebrospinal meningitis (old) without signs, 64 per cent had marked findings in the cerebrospinal fluid, and 28 mild findings; the rest were negative.

18. In paresis all the findings were marked.

19. Transverse myelitis, multiple sclerosis, and progressive muscular atrophy should always be investigated for syphilis.

20. Tabes dorsalis was divided into five groups: (1) Marked findings in both blood and cerebrospinal fluid. (2) Positive blood and mild findings in the fluid. (3) Positive blood and negative spinal fluid. (4) Negative blood and positive spinal fluid, and those showing the paretic curve.

21. The intensity of the serologic findings is an index to the activity of the syphilis.

22. The so-called paretic curve may occur in any Lange test, no matter what type of activity, if the process is very active.

## THE TECHNIC OF THE BORDET-WASSERMANN REACTION\*

### A CONSIDERATION OF THE PROBLEMS INVOLVED IN ITS STANDARDIZATION

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IT is safe to say that of all the laboratory tests now available to the general medical profession, whether chemical, bacteriologic or serologic, none has proved itself of such great value at the present time, or offers such great possibilities for the future, as the Bordet-Wassermann reaction. It is quite true that only in the larger centers of population has it had, up to the present, a wide application; and, as a consequence, the statement just made will sound somewhat extravagant to those practitioners from outside points who have not been closely in touch with such work. It is not yet realized by many physicians that syphilis may be the underlying cause of many conditions which are so obscure as regards diagnosis, and so obstinate in yielding to symptomatic treatment.

A wider application of the test would not only reveal the secret in many of these puzzling cases, but would prove of great eliminative value where the result is negative. Add to this the other, larger sphere of this laboratory procedure, that of ascertaining in a scientific and reliable way, the progress of a syphilitic patient under treatment. Too few physicians avail themselves of this valuable guide in treatment and prognosis.

Unlike the Widal test, or other diagnostic methods of the laboratory, the Bordet-Wassermann reaction is complicated in the preparation of the reagents, the carrying out of the technic and the interpretation of the results. It is not to be wondered at, therefore, that many deviations from the original method have been described by various workers, who claim special advantages for their respective modifications. These alleged advantages may be divided conveniently into two classes:

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I. Those claiming a more delicate or accurate diagnosis.

II. Those claiming a simplified technic, designed to reduce the labor involved in making the test.

It is not within the compass of this paper to describe these various methods in detail, but mention will be made from time to time of some of the important modifications while discussing the different subjects in their proper order.

It may be well to analyze our objects in performing the Wassermann test. First of all we desire to detect every case of syphilis. Secondly, we consider it equally essential to detect the absence of syphilis in all cases not infected. Extremists are always to be found in the medical profession, and among the champions of the Bordet-Wassermann reaction there are a few enthusiasts who claim for it almost supernatural powers. On the other hand, there are some<sup>1</sup> (and their numbers are significantly few) who claim very little specificity for the test. In a calm consideration of the whole matter one must realize that there is no diagnostic method, clinical or laboratory, known to medical science, which is infallible. The percentage of error is not only due to technic and its limitations, but there is no doubt that the personal element enters largely into the question, and as Ottenberg<sup>2</sup> says, some good workers obtain satisfactory results in using inferior methods, simply because of skill and experience in using the method.

It is, however, both startling and gratifying to find such an unexpected uniformity of results as now exists in the different laboratories, and this knowledge should act as a spur to encourage the workers to standardize their technic and thus place the test upon the highest scientific plane.

Let us now consider what is involved in the effort to detect every case of syphilis. Viewing the problem from a biologic standpoint, it is not difficult to understand that during the first two, or even three weeks, after the appearance of the initial sore, the test is very often negative in true cases of syphilis. The so-called syphilitic antibody requires time for its production, and it would be unreasonable to expect a positive test before its appearance in the blood. Passing on then, to the time when one should reasonably expect the presence of the antibody in the blood, several factors have an important bearing upon the result of the test. Approximately one hundred per

cent of all cases of frank secondary syphilis give a positive reaction by any of the well recognized methods. It is in the tertiary and latent stages, as well as in cases involving the nervous system, that diversity of results appear according to the technic employed. To these must be added cases of known syphilis which are undergoing, or have undergone, treatment. One of the most potent causes of this diversity is the difference in antigen used. It is almost universally agreed that a cholesterinized heart antigen is much more sensitive than a simple heart antigen. The question we have to decide is, which, if either, is the accurate one? Then, too, comes the strength of the hemolytic system used. It must be decided as to what maximum strength is permissible without danger of losing the delicacy required to detect weakly positive cases. This factor is just as important as our determination of the minimum strength compatible with safety as regards specificity of fixation. These points, together with details concerning the actual technic employed, are matters which must be left to the judgment of the investigator and are therefore more or less arbitrary. With these significant facts before us, it is not difficult to appreciate the obstacles confronting an attempt to standardize the whole procedure. It is the purpose of this paper to take up each point in detail, to present the actual findings, and to draw, therefrom, conclusions which it is hoped, will be of value to the workers in public health laboratories.

For the sake of uniformity we shall assume from the beginning that the total volume in each tube at the end of the reaction is 2.5 c.c. It is true that in the original tests Wassermann used 5 c.c. and it is also true that some laboratories now use very small amounts in an effort to economize in the reagents. Most laboratories now use 2.5 c.c. as the optimum volume, believing that it combines reasonable accuracy with proper economy in reagents. This view coincides with my own personal experience.

#### THE ANTIGEN

As I have intimated above, the question of the antigen is a difficult one to solve. The choice of antigen lies, in the opinion of the great majority of workers, between the simple alcoholic extract of heart, and the cholesterin reinforced alcoholic extract of heart. It must be noted, however, that some laboratories, for one reason or another,

use the acetone-insoluble fraction of the simple alcoholic extract of heart muscle according to the method of Noguchi. I have had no personal experience with Noguchi's antigen and shall refrain from comment which would only be based on second-hand information.

The simple alcoholic extract of guinea pig and beef heart has many advocates<sup>3</sup> and with good reason. Ottenberg compares the results obtained with such an antigen with those using a cholesterin reinforced alcoholic extract. In 95 per cent of the cases the results were identical. Of the 67 disagreements in 1,241 cases, 42 gave definite positive reactions with cholesterin, and negative or doubtful reactions with the simple antigen. Of these, he says, 22 were cases in which there was no reason to suspect syphilis. Taking the other 25 disagreements, the cholesterinized antigen gave negative results, while the simple alcoholic extract yielded positive tests. Twenty of these were known or highly probable cases of syphilis, while five were doubtful cases in which syphilis could not be excluded. He admits, however, that the cholesterin antigen gives a "far greater number" of weak positive reactions in treated syphilis, though he claims that this advantage is counterbalanced by a considerable number of false positive reactions. He, therefore, draws the conclusion that "cholesterin reinforced antigen should never be relied on alone for diagnosis."

Let us now analyze the data on which he forms this opinion. First of all, there are 95 per cent of agreements between the two antigens. Of the 5 per cent remaining, the cholesterin antigen gave positive reactions in slightly over 3 per cent of the total, leaving less than 2 per cent to the credit of the simple extract. About half of the cholesterin positive disputed cases were undoubted or possible cases of syphilis, which brings the error with that antigen, according to this observer, down to slightly over 3 per cent as compared with an error of slightly less than 3 per cent with the simple antigen. So far the advantage is to a very small extent in favor of the latter.

Deduct from this, however, the very important drawback in not being able to detect many cases of treated syphilis. Remember also that 18 of the 22 alleged false reactions charged against the cholesterin antigen were cases of pregnancy which, as has been shown in our laboratory, can easily be ruled out by repeating the test after parturition. Furthermore, where routine tests are made in a large hos-

pital, it is a matter of common experience that many cases of syphilis are latent—presenting no symptoms or signs, and giving no history of infection. Such instances are so common that one is quite justified in concluding that of the twenty-two in which Ottenberg could find no reason to suspect syphilis, some of them at least were undoubtedly cases of that disease.

Stokes and O'Leary<sup>4</sup> find that in nearly every instance of provocative Wassermann tests, the cholesterin antigen alone was successful in detecting positive cases.

One more point is worthy of consideration before leaving this question; namely, the statement already indirectly referred to, that in 25 cases the simple antigen yielded a positive result, while the cholesterin antigen results were negative. No explanation of this phenomenon is advanced, and indeed none suggests itself to me. It seems difficult to understand why an antigen made up in exactly the same way, but with the additional safeguard against false negatives provided by cholesterin, should fail to be as sensitive. Nor has this phenomenon occurred in our laboratory, although it must be admitted that we have not yet made as many tests in parallel as has Ottenberg.

In reporting such a series of cases, it is important to state whether they were done in routine or whether done on suspected cases. In the former instance there will necessarily be a great many negatives with a correspondingly great number of agreements; while in the latter, there will be many positive tests, with a greater opportunity for the results of the two methods to be at variance. In a series of 300 cases, of which 85 were positive, we found 85 positive with the cholesterin antigen, and 68 with the simple alcoholic extract. All the 68 were found to be among the 85 cholesterin positive cases. Thus 17 cases were negative with simple antigen and positive with cholesterin, and in all these there was no reason to believe they were not syphilitic. Nine had been treated and two were early primary syphilis. Besides the 17 that altogether escaped detection with the simple antigen, there were 28 in which the reaction, while positive, was weaker with the simple antigen. Of these, 8 had been treated, and 2 others were early cases of primary syphilis.

Of the total 45 disagreements between the two antigens, with one exception, all were in favor of the cholesterin reinforced extract.

In this single exception, a treated case gave a 430 reaction with the simple, and 320 with the reinforced antigen. This is the only instance of the kind occurring in my experience, even aside from the series now being reported, and may be due to an error on the part of the technician. Certainly no other explanation seems plausible.

The figures quoted above were obtained by the regular procedure in the case of the cholesterin antigen, and primary incubation for four hours in the ice chest in the case of the simple extract. With the ordinary primary incubation of one hour in the incubator the simple antigen gave still less reliable results.

TABLE I  
SUMMARY OF DISAGREEMENTS\*

	CHOLESTERIN ANTIGEN	SIMPLE ANTIGEN	TOTAL
Number positive	85	68	85
Treated, but positive	17	12	17
Early chancre, but positive	4	2	4
Reaction strongest (treated cases)	16	1	17

The experience of Thomas and Ivy<sup>5</sup> corroborates our own. It may be worth suggesting, therefore, that before such a statement as that of Ottenberg be given full credence, control tests with more than one cholesterin antigen, or duplicate tests with the same antigen, be made, for it is possible that the variance in the results may be due to differences in technic or even to oversight on the part of the laboratory workers.

To sum up, then, the balance seems to be definitely in favor of the cholesterin reinforced antigen, to be used, of course, only by experienced workers. There is something to be said, it is true, in favor of using both as a check one upon the other. Here too, however, it is liable to lead to confusion and doubt in the mind of the worker, who must then decide upon which result he should place his reliance. Personally, I believe that if a worker uses both antigens, the simple antigen should only be considered of value, as *directing his attention* to those cases giving positive results with the reinforced antigen alone, so that he may inquire more minutely into the clinical

\*The figures in this table refer to *disagreements* only. Both antigens were made at the same time, from the same heart. Note how closely the figures in the total correspond to the figures of the cholesterin antigen.

history, and if desirable, as in the case of pregnancy, febrile conditions and certain tropical diseases, arrange for a further examination of the blood at a later date.

As to the dosage of antigen, the reader is directed, for an admirable summary of the facts concerning this question, to Ottenberg's paper, to which reference has already been made. It is sufficient to say that in our own laboratory the dosage is determined by two main factors; namely, the anticomplementary power, and the specific binding power. No antigen is considered satisfactory which is at all anticomplementary in a dilution of one in eight, and which does not give a positive reaction with pooled positive sera in a dilution of one in eighty. This gives a wide range, and a point is taken midway between these two extremes, generally one in twenty, of which 0.5 c.c. is used in the test. These remarks apply to a cholesterinized human heart antigen.

#### THE ALEXIN, OR COMPLEMENT

The next problem to discuss is that of the dosage of complement. For convenience, it is customary to dilute the guinea pig serum one in ten with saline, and many laboratories use a fixed amount (usually 0.5 c.c.) of this dilution throughout the test. It is true, however, that guinea pig serum varies as to its complement content, and this necessitates the adjustment of the amboceptor to meet the variation. To accomplish this, varying amounts of amboceptor are titrated with a fixed arbitrary amount of complement (0.5 c.c. of 1:10 dilution). Such a method means that instead of increasing the amount of complement when it is weaker than usual, the amboceptor is increased. This procedure is possible owing to the fact that within certain limits the results appear the same. Many laboratories, among them those of Bruck and Citron, follow this method. It seems, however, more reasonable to vary the amount of the reagent, which itself is not constant in quality. We know that the hemolysin is remarkably stable, whereas it is a matter of common experience to find certain guinea pigs whose blood shows a low complement content.

A number of workers, including McIntosh and Fildes, Thomas and Ivy, Walker and Swift, Boas, Ottenberg, use, therefore, fixed amounts of amboceptor and vary the amount of complement according to its strength.

The advantage of the former method is one of economy of time, inasmuch as the addition of complement to the tests need not be deferred until the titration of that reagent is completed. On the other hand, as Ottenberg points out, a weak complement may be supplemented, quite properly, in the second part of the reaction by an excess of amboceptor, but this still means that during the first incubation (the fixation period) we have a deficient complement as compared with an experiment in which the quality of that reagent is up to the average. So that no matter how one varies the amboceptor, it does not have the effect of keeping the complement in the test proper at a constant level.

Granting then, that it is more logical to titrate the complement each day, the question arises as to the method of determining the unit. Wassermann took 1 c.c. of the 1 in 10 dilution, which would bring the amount to 0.5 c.c. in performing the test in half quantities as we prefer. Let us now see how this compares with the results on titrating the complement.

Using an amboceptor which has been titrated and used many times previously with different complements from day to day, the average result of several representative titrations with different satisfactory complements, is taken as the unit. This usually is 0.1 to 0.15 c.c. of a 1:300 dilution of amboceptor (the amount, of course, varies with the titer of the serum of the rabbit from which the hemolysin has been obtained). Let us assume it is 0.1 c.c. That is called the unit of this particular amboceptor, and is stationary so long as the amboceptor lasts, provided it does not become infected. Having determined the unit, a series of tubes is set up, each containing two and one-half units of amboceptor with varying amounts of complement. If the same complement is used in this test as in the previous one, it will be found that the complement titer will be approximately two and a half times less than the amount used in determining the amboceptor titer. This observation coincides with that of Ottenberg in the earlier part of his paper<sup>6</sup> but contradicts a later statement of the same author. The explanation of this apparent inconsistency seems to be that his arbitrary amount of complement is too low to produce the effect to which he calls attention. In other words it is too near the minimal dose. I have repeated the experiments he outlines many times and at no time have I obtained the

results he indicates. The following is the nearest I could get to his findings:

I. Complement 1 in 10, 1 c.c.

Sheep's corpuscles 5%, 1 c.c.

Amboceptor (1:300)	0.0	0.05	0.1	0.15	0.2	0.25
Air incubation for 1 hour at 37° C.	N.H.	N.H.	P.H.	P.H.	C.H.†	C.H.*

The unit was, therefore, between 0.2 c.c. and 0.25 c.c. and was taken as 0.22 c.c. Two units of this amboceptor were now titrated against the same complement.

II. Amboceptor 0.44 c.c.

Sheep's corpuscles 5%, 1 c.c.

Complement 1-10	0.3	0.35	0.4	0.5
Air incubation for 1 hour at 37° C.	P.H.	P.H.	A.C.H.†	C.H.

Thus we see that the unit is 0.5 c.c., or nearly so.

By this it is apparent that the two titrations correspond very markedly, and any difference, while tending towards Ottenberg's contention, is very small.

Our own daily titrations are carried out in much the same fashion. The following is a typical example:

Sept. 7, 1917

I. Complement 1 in 10, 0.5 c.c.

Sheep's corpuscles 5%, 0.5 c.c.

Amboceptor (1:30°)	0.0	0.05	0.1	0.15	0.2
Air incubation for 1 hour at 37° C.	N.H.	C.H.†	C.H.	C.H.	C.H.
Unit = 0.6 c.c.					

II. Amboceptor two and one-half units (0.15 c.c.)

Sheep's cells 5%, 0.5 c.c.

Complement, 1 in 10	0.1	0.15	0.2	0.25	0.3
Reading after 1 hour at 37° C.	P.H.	P.H.	C.H.	C.H.	C.H.

The unit of complement is thus seen to be 0.2 c.c.

Note how closely Experiment I and II correspond. By multiplying the amboceptor by 2.5, the complement is divided by 2.5.

Variations from this result are infrequent and are generally very minor. They probably are caused by slight errors in technic, as for example, allowing a drop or two of complement to escape from the pipette while withdrawing it from the tube.

\*N.H., No hemolysis; P.H., Partial hemolysis; C.H., Complete hemolysis.

†Almost complete hemolysis.



Having determined the unit of complement in this way, it now becomes necessary to decide the number of units to be used in the test proper, for after all, this is one of the most important factors in influencing the delicacy of the reaction. Nearly all the workers who do not use a fixed dose of complement employ two units or less. Browning and McKenzie, however, advocate very large amounts,—7, 10, 15, 20, 30, 40 units, and Field, 6 to 8 units. These quantities we have found, as have others, to be too large. Two units seem to be very suitable with a simple heart antigen, but with a cholesterinized extract we have found at least 2.5 units to be necessary, while for regular routine 3 units seem advisable, since with the former amount, there is sometimes a small amount of nonspecific fixation with certain sera.

The difference between two units as determined by titrating against one unit of amboceptor, and 2.5 units as determined by titrating against 2.5 units of amboceptor, is considerable, so that the actual amounts used by us are somewhat less than those employed by Walker<sup>7</sup> and Swift, (approximately 12 per cent less). The reason is found in the fact that by this method we are able to follow the treated cases much further. Two units of complement as determined by titrating against two units of amboceptor is actually the same as 2.5 units of complement as determined by titrating against 2.5 units of amboceptor. Three units of complement as determined by the latter method (as employed in our laboratory) is equivalent in actual amount of guinea pig serum to 2.4 units as determined by the former.

The method of Thomas and Ivy theoretically has much to commend it. They use in the test the smallest amount of complement which will give complete hemolysis when titrated in the presence of the regular amount of antigen, and pooled negative serum. In other words, they estimate the anticomplementary power of the serum, and of the antigen serum combination, and arrange for the presence in the test of one unit of complement over and above the amount fixed nonspecifically by these reagents. Ottenberg uses the next dose above that which just gives complete hemolysis in order to increase the margin of safety.

We have tried this method in parallel with our regular procedure, and must confess that while the results with both were consistent,

save in minor details, the readings of our own method were more definite, and while we are still using this modification along with our own for purposes of comparison, we can not at present feel towards it the same confidence that the regular procedure inspires. It deserves, nevertheless, a longer trial under impartial control before being definitely pronounced inferior.

Before we close this discussion of the complement, mention must be made of a peculiarity of some specimens of guinea pig serum; namely, that they are not nearly so amenable to fixation as are others. Browning and McKenzie showed this in 1909, and Ottenberg also calls attention to it. The latter author has been working at the problem with a view to devising a method whereby the fixability of the complement may be measured in the preliminary titration. Until some such scheme is evolved, the only means of avoiding trouble from this source is by using for each day's test a large number of guinea pigs, thus minimizing the effect, should one of the sera prove weak in this regard.

#### AMBOCEPTOR TITRATIONS

The first question to decide is the length of time to be allowed in the thermostat for the titration. Varying from fifteen minutes (Field, Kaliski), half an hour (Sormani), one hour (Wassermann, Walker and Swift, Thomas and Ivy), two hours (Boas, Thomsen, Noguchi), the time employed by the different workers shows little uniformity. Using the air incubator at 37° C. one finds that hemolysis rarely begins before eight or ten minutes, and while it is more than half completed in thirty minutes, one hour elapses before the process actually ceases. Sometimes, indeed, on leaving the mixtures exposed for a longer period, a further laking occurs, but it is very slight and it is difficult to see any real advantage in so doing. Shorter periods than one hour are probably justified when using the water-bath, since by that method the tubes and their contents reach the required temperature much more quickly. There is another advantage in the use of the water-bath; namely, that constancy in temperature can be more easily secured, unless, as in our laboratory, a very large incubator is available, enabling one to open the doors without an appreciable change in temperature.

If preliminary sensitization of the corpuscles is carried out in the

actual test, it is equally important to follow this technic in the preliminary titration. This may be accomplished by mixing the amboceptor and cells and allowing them to stand in the incubator for fifteen minutes before setting up the test.

#### SHEEP CELL SUSPENSION

Many laboratories obtain their supply of sheep cells from an abattoir and thus are dealing with entirely different corpuscles each day. As has been shown by Ottenberg and Hopkins,<sup>8</sup> cells of individual sheep vary considerably in their resistance to hemolysis. It would, therefore, seem advisable that one, or if necessary, two sheep be kept for this purpose.

Of more importance is the question of the preparation of the cell suspension. The original method was to wash the corpuscles with saline, by centrifugalization. This was done three times, and after the supernatant fluid had been pipetted off the last time, the cells were restored to the original volume of the blood by the addition of saline solution. This suspension was then diluted 1 in 20 with saline, making a 5 per cent emulsion. Some workers, as Browning and McKenzie and Citron, still adhere to this method, but the great majority have discarded it for a modification which seems an improvement. It is merely to make a 5 per cent suspension of the sedimented corpuscles after pipetting off the supernatant fluid. It is held, and with good reason, that the corpuscle content of the blood of different sheep, or even of the same sheep upon repeated bleedings, varies. According to the old method, this would result in varying concentration in the suspensions used. By centrifuging in the same machine at the same speed for a definite length of time, one can obtain a uniform sediment regardless of the corpuscle content of the blood.

An antihuman hemolytic system may be substituted if desired. It does not seem to alter the test in any way, and is often more practicable, especially in small laboratories where the expense of keeping sheep on hand would be out of proportion to the advantage gained.

#### PATIENT'S SERUM

The amount of serum used in the test seems to be fairly uniform throughout the different laboratories. Many use 0.1 c.c. in the

test proper, although Wassermann gave 0.2 c.c. as the proper quantity. Personally we follow the method of Boas of employing three tubes containing 0.2 c.c., 0.1 c.c. and 0.05 c.c. respectively. This allows of a more accurate estimation of the strength of the reaction and does not involve a prohibitive amount of labor.

Inactivation of the serum at 56° C. for half an hour in a water-bath is carried out in most laboratories as a routine measure. The objects of this procedure are two; to destroy the complement in the patient's serum, and to remove the unknown substances which render certain sera anticomplementary.

It was also reported<sup>9</sup> that active serum yielded false positive reactions. Noguchi pointed out that this was due to impurities in the antigen and claimed that active serum used in combination with his acetone-insoluble lipoids precipitated from the alcoholic extract did not give these false positive results. His method, however, has not come into general use, and for the present, at any rate, it seems advisable to adhere to the practice of inactivating the serum.

#### NATURAL AMBOCEPTOR IN THE PATIENT'S SERUM

It is a matter of common observation that many human sera contain appreciable amounts of antish sheep hemolysin, and some contain quite large amounts. Some workers use an extra tube in the test in which they omit the amboceptor, and if laking occurs, they may absorb the hemolysin and repeat the test.

In Noguchi's modification, by using an antihuman hemolytic system, this factor is obviated. We have carried out a considerable number of experiments in regard to natural hemolysin, and have corroborated the statements of Wassermann, Neisser, Bruck, and Schuct,<sup>10</sup> and others, concerning its occurrence. We have performed many tests, using the extra tube for the purpose of detecting its presence, and in all instances of negative results with evidence of a considerable amount of natural amboceptor, the serum was treated with sheep cells and then the test repeated. In no case in the series, was there any difference in the result.

True enough, we not infrequently find evidence of natural amboceptor in the first and second, even in the third tube of the main test, but it seems never to occur in such large quantities as to cause complete hemolysis in a positive serum in the third tube

(which contains only 0.05 c.c. serum). Therefore, when we find a test in which the tube containing 0.2 c.c. serum shows partial or complete hemolysis, the second tube showing less hemolysis, and the third tube (containing 0.05 c.c. serum) still less, or none at all, we immediately suspect the presence of natural amboceptor and proceed to absorb it before repeating the test. Our position regarding the presence of natural amboceptor in the patient's serum is upheld by other authorities, notably Neill,<sup>11</sup> who states in a communication published since the above was written, that from his experiments he concludes that the presence of antishoop amboceptor in sera does not yield false results where not less than 0.1 c.c. of serum is used for the test.

Just here it may be well to call attention to some peculiar substance present in some sera, which causes hemolysis in exactly the same fashion, but which is not removed on exposure to sheep cells. Others<sup>12</sup> have noted the same phenomenon, but so far no explanation has been offered.

#### PRIMARY INCUBATION

The majority of workers follow the method of Bordet and Gengou, and of Wassermann, in the primary incubation; that is, one hour in the air incubator at 37° C. In 1913, Jacobsthal<sup>13</sup> reported that ice box incubation at 8 to 10° C. for three or four hours gave better results. Since that time, his statements have been confirmed by many others, but lately the matter has come into prominence by the work of Koopman, Ottenberg, and still more recently by Smith and MacNeal,<sup>14</sup> who find that with ice box incubation for four hours the results with simple alcoholic extracts are just as delicate as those with cholesterinized extract in the air incubator at 37° C. We have found the ice box method to be of decided advantage in using the simple heart extract, and would strongly recommend its use if this antigen is to be employed. The ice box, however, is quite unsuitable for use with the cholesterinized extract and as long as we employ this antigen, we shall adhere to the air incubator method.

#### THE SERUM CONTROL TUBE

According to the method laid down by Wassermann, and followed by the majority of workers, the amount of serum in the con-

trol tube is double that contained in the tubes of the test proper, or, as in our laboratory, where there are three tubes, the control contains twice the amount of serum in the first tube (0.2 c.c). Speaking from a large experience with cholesterinized antigen, I can not agree with Ottenberg that the control tube containing a double dose of serum does not form an additional factor of safety. If, as I have argued above, the natural amboceptor is not giving us false negatives, his contention that this property of the serum robs it of its value when used in double quantity, does not hold.

The same amount of complement is added to the serum control tube as to the others. Thomas and Ivy, Browning and McKenzie, and Ottenberg question the advisability of this, holding that there is an excess of complement, and thus slightly anticomplementary sera may be taken as weak positives because the control tube goes perfectly clear. Their contention is probably of importance where their method of using a single dose of serum in the control tube is followed. It is worthy of consideration even where a double dose is used. The means they employ (that of titrating pooled negative sera with complement) to ascertain the anticomplementary power of the serum so as to measure the minimal dose of complement for the control tube is open to criticism, for it assumes that the average will suffice, whereas, approximately half the sera will have a higher anticomplementary power than the one given by their test.

The ideal way would be to test each serum for anticomplementary power, and then add just sufficient complement to clear the tube. This, however, would involve a prohibitory amount of time and labor, and the advantage would not justify it.

In our laboratory, it is found that by performing the test with a properly adjusted hemolytic system little difficulty is experienced in this regard. In spite of this, however, there are occasionally a few sera which exhibit a slight inhibition, with the control tube perfectly clear. Where the case is not one of early primary syphilis, or an older case which has been treated, we believe all these slight inhibitions to be nonspecific and this view is based on practical experience. We, therefore, never interpret a test as positive unless it is very strongly positive, in other words, complete inhibition of hemolysis in all three dilutions of serum. Such a case is recorded as a 444 reaction. Each 4 represents one dilution of serum, and the three

figures indicate exactly as much as if we had written + + + +, + + + +, + + + +. After treatment, the third tube may show 50 per cent hemolysis, while the remaining tubes may still show complete inhibition. Such a result would be recorded 442. The serum under treatment may go all the way from 444 to 000 (negative) as illustrated in the following case:

TABLE II  
CASE A. K. UNDER TREATMENT WITH DIARSENOL

Sept. 14, 1917	No treatment	Wassermann	444
Sept. 21, "	After one diarsenol	"	444
Sept. 26, "	After two diarsenols	"	444
Nov. 2, "	After three diarsenols	"	430
Nov. 7, "	After four diarsenols	"	320
Dec. 3, "	After five diarsenols	"	000

We claim for this method of interpretation (originated by Major Duncan Graham, head of this laboratory) that the clinician can see exactly what the technician in the laboratory has found in the test. It is not as cumbersome as the + + + + method and gives more information. Craig<sup>15</sup> uses only one dilution of serum (0.1 c.c.) and, therefore, can only say whether a patient's blood is positive or negative. He can not, however, detect early change due to treatment, nor can he follow his treated cases as long as can be done by having one tube containing 0.2 c.c. of serum.

A complete series of examples of titrations and tests will be appended in order that there may be no doubt left in the mind of anyone regarding the method now employed in our laboratory.

This method has proved satisfactory in many thousands of cases, and while it is not by any means infallible, in our hands, it is superior to any other method we have tried so far.

#### I. TITRATION OF NEW AMBOCEPTOR

Dilutions of the rabbit's serum are made as follows: 1:100, 1:500, 1:1000, 1:1500, 1:1200; 1:2500 and 1:3000.

To 0.5 c.c. of each dilution are added 0.5 c.c. of a known average strength complement, and 0.5 c.c. 5 per cent sheep's corpuscles.

Each tube is made up to 2.5 c.c. with saline, and the whole is incubated for 1 hour at 37° C. in air.

The titer of the hemolysin is taken as the highest dilution which yields complete hemolysis.

The rabbit's serum is then kept in sealed tubes and diluted from time to time to such an extent that the unit as determined by titration against 2.5 units of complement is somewhere about 0.1 to 0.2 c.c.

## II. TITRATION OF NEW ANTIGEN

A. For nonspecific binding (anticomplementary power).

Dilutions of antigen are prepared: 1:2, 1:4, 1:6, 1:8, 1:12, 1:16, 1:20.

To 0.5 c.c. of each dilution are added three units of complement and saline to 1.5 c.c.

Incubation in air at 37° C. for 1 hour.

One c.c. sensitized sheep's corpuscles is then added and incubation for 1 hour in air at 37° C. is repeated.

The highest dilution in which there are unlysed cells remaining, is taken as the anticomplementary power of the antigen. This is usually 1:4.

B. For specific binding power.

Dilutions of antigen are prepared as follows: 1:30, 1:40, 1:60, 1:80, 1:100, 1:120, 1:140. To 0.5 c.c. of each dilution are added three units of complement, 0.1 c.c. pooled positive serum and saline to 1.5 c.c.

Air incubation at 37° C. for 1 hour.

One c.c. sensitized sheep cells is added, and the reading taken after 1 hour in air incubator at 37° C.

The highest dilution of antigen giving complete inhibition of hemolysis is taken as the specific binding power of the antigen. It is usually 1:100 to 1:120.

## III. DAILY TITRATION OF COMPLEMENT

Amboceptor, 2.5 units in each tube excepting the control tube.

Sheep's cells 5 per cent 0.5 c.c.

Complement 1:10, 0.1 c.c., 0.15 c.c., 0.2 c.c., 0.25 c.c., 0.3 c.c. control tube, 0.5 c.c.

Saline to make 2.5 c.c. in each tube.

Read after 1 hour in air incubator at 37° C.

The unit of complement is taken as the smallest amount of complement which will completely hemolyze the red blood cells.

Three units of complement are used in the Wassermann test.



TABLE III  
ACTUAL BORDET-WASSERMANN TEST

UNKNOWN PATIENT'S SERUM	ANTIGEN	COMPLE- MENT	SALINE	Air incubation at 37° C. for 1 hour	SENSITIZED CORPUSCLES	Air incubation at 37° C. for 1 hour	RESULTS
Tube I 0.2 c.c.	0.5 c.c.	3 units	Up to 1.5 c.c.		1 c.c.		?
Tube II 0.1 c.c.	0.5 c.c.	3 units	Up to 1.5 c.c.		1 c.c.		?
Tube III 0.05 c.c.	0.5 c.c.	3 units	Up to 1.5 c.c.		1 c.c.		?
Tube IV 0.4 c.c.	—	3 units	Up to 1.5 c.c.		1 c.c.		Complete hemolysis
KNOWN POSITIVE SERUM							
0.1 c.c.	0.5 c.c.	3 units	Up to 1.5 c.c.		1 c.c.		No hemolysis
0.2 c.c.	—	3 units	Up to 1.5 c.c.		1 c.c.		Complete hemolysis
KNOWN NEGATIVE SERUM							
0.2 c.c.	0.5 c.c.	3 units	Up to 1.5 c.c.		1 c.c.		Complete hemolysis

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## THE TREATMENT OF EARLY SYPHILIS IN RELATION TO THE DEVELOPMENT OF NEUROSYPHILIS\*

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MODERN work on the treatment of general paresis, such as that of Solomon at this hospital, has clearly shown that there are cases which for some as yet unknown reason do not improve; or, if they improve, relapses are early and marked. Similarly there are cases in which vigorous treatment in the early stages of syphilis will not prevent the later development of paresis.

The difficulty of obtaining from cases of neurosyphilis accurate histories regarding syphilitic infection and symptoms, is well known. Still less often are we able to obtain any accurate information regarding the precise amount and character of antisyphilitic treatment at the time of infection. Accordingly the cases reported here should be of general interest because of the known amount and character of the treatment. A further interesting and suggestive point lies in the results of the type of treatment developed and applied by Solomon. This seems to me to carry a wholesome therapeutic lesson.

*Case I.*—A male, age 28, came voluntarily to the hospital December 11, 1916, complaining of loss of memory, speech difficulty, and irritability, all developed within the six months just past. He was tidy, elated, showed a mild memory defect, was somewhat silly, over-emotional; circumstantial; rather wandering in his attention, and had a speech defect. Physical examination was not remarkable except pupils unequal, irregular, and react sluggishly; tendon reflexes hyperactive; no sensory disturbance or ataxia.

Six years previously he had a chancre. During five years he

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\*Contribution of the Massachusetts Commission on Mental Diseases, whole number 203 (1917.23). The previous contribution 202 (1917.22) was by Donald Gregg, entitled "The Differentiation of Psychotic and Neurotic Conditions" (to appear in Boston Medical and Surgical Journal).

received almost continuous treatment with mercury by injection. He had two injections of salvarsan. He never received any potassium iodide. He never showed any secondary symptoms.

*Laboratory Findings:* blood and fluid Wassermann reaction positive. Spinal fluid showed: globulin 3; albumin 4; cells 34; and a gold reading of 5555431000.

In twelve days he received four injections, totaling 2.3 grams of diarsenol. He was then discharged to the out-patient department, where treatment was continued, so that on February 14, 1917, the Wassermann reaction on the blood serum was negative, and the spinal fluid showed: globulin 2; albumin 3; cells 4; gold reading, 2222210000. In the meantime there had been great physical and mental improvement. At the present time he shows slight tremors; a little stumbling on test phrases, but his ordinary speech is clear and accurate; his memory is good; and his insight into his past illness is good.

This case presented a clinical symptom-complex typical of paresis in its early stages coming on six years after the initial lesion, and after five years of rather intensive treatment. He has shown marked improvement under the type of treatment which has produced the best results in paresis, but the favorable time for such intensive treatment was months or even years ago, before the changes in the nervous system had advanced to any degree of degeneration.

*Case II.*—A male, age 34, came voluntarily to the hospital May 7, 1917, complaining that for about six months he had been tired, irritable, and nervous, and was getting worse. He also recognized a memory loss. He worked in a post office at night and had spent his days for two years as a medical student. Normally ambitious, and a hard worker, he has worried a great deal over his condition; has become emotionally unstable, crying readily, depressed, and showing memory loss. Aside from exaggeration of the knee-jerks, and a very slight speech defect, the physical examination was negative.

He had a chancre three years ago. After the secondary symptoms appeared, he received thorough and intensive treatment with salvarsan, mercury, and potassium iodide. Mercury and potassium iodide have been carried in courses up to the time of admission. Of late he has been troubled a great deal by headaches. A part of his difficulty in medical school, where he did not do very well, may have

been due to the spirochetal invasion of the central nervous system, though undoubtedly much of it was due to his combinations of work.

*Laboratory Findings:* Wassermann reaction on the blood and fluid positive. The spinal fluid showed: globulin 2; albumin 2; cells 8; and a gold reading of 5554332100. Under intensive treatment of the usual type, his mental and physical condition improved very markedly, and on July 21 the spinal fluid showed: globulin 0; albumin 0; cells 0; gold—negative.

At the present time, aside from slight memory loss and some slowing in his work, his condition is very good.

*Case III.*—A male, age 43, was brought to the hospital by the police on August 16, 1916. He was then in a highly excited state, grandiose and talkative. On examination he was oriented; active; euphoric; voluble; there was some flight of ideas; and he had no insight.

*Physical Examination.*—The pupils were unequal, irregular, Argyll-Robertson in type; the tendon reflexes were absent; there was some incoordination; he had a high blood pressure.

At 27, sixteen years ago, he had a chancre. During the succeeding ten years he was treated almost continually with mercury and iodide. The principal reason for this was the frequent recurrence of skin symptoms. When salvarsan was introduced he was among the first in Boston to receive it. With this treatment his skin lesions healed. Then for six years treatment was not so intensive. Despite all of this treatment, and the marked skin lesions (which are sometimes supposed to argue against the later development of neurosyphilis), he eventually developed paresis. Under intensive treatment he improved sufficiently to go on a visit in November, remaining out for a year. He was then returned in a maniacal state, having refused treatment for six months before readmission.

At the time of his first admission, the laboratory findings were: blood and spinal fluid Wassermann reaction positive. The spinal fluid showed: globulin 3; albumin 2; cells 8; and a gold reading of 5555432100.

Despite the clinical improvement under treatment, the spinal fluid always remained positive to the various tests.

These cases do not add much to the solution of the important

theoretical and practical question: "Why does any syphilitic have neurosyphilis?"—but they do demonstrate the fact that, either because of special invasive powers or increased susceptibility of the nervous system, neurosyphilis may develop despite thorough remedial measures. They show very clearly that it is not a question of time interval after infection, or after cessation of treatment, since the interval between infection and paresis was three, six, and sixteen years, respectively.

These cases bring sharply to the fore a question concerning the duty of the syphilographer to his patient. It is my belief that before being discharged from treatment, all syphilitics should have lumbar puncture to determine the condition of the spinal fluid. Certainly all patients who suffer much from headache, or show any neurologic or mental changes, however slight, should be punctured. If the fluid tests are positive, then treatment should be modified accordingly. Furthermore, if intensive treatment of the patient after paresis has developed will bring about an improvement, then intensive treatment is certainly indicated in all cases showing any changes in the spinal fluid, and the spinal fluid findings should be the guide in further treatment.

#### CONCLUSIONS

Thorough, early treatment is not a guarantee against later paresis. The time interval between infection and development of paresis is not especially modified by the usual treatment. Whether due to special invasive powers, lack of resistance in the nervous system, or drug-fastness of the organism, the fact remains that there are cases in which the most vigorous treatment fails to prevent the development of paresis, or even to delay it.

Patients in the secondary stages should be punctured, and treatment modified according to spinal fluid findings. If not all patients, then certainly all early syphilitics with headache or any nervous or mental symptoms, should be punctured.

If intensive treatment will improve the patient who has developed paresis, then intensive treatment of the same type months or years before, guided by spinal fluid findings, should go far towards preventing the later development of paresis.

## THE SYPHILIS CLINIC OF EMORY UNIVERSITY, ATLANTA, GA.

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FOR the first time in the history of the Atlanta Medical College, Department of Medicine of Emory University, syphilis has come into its own. It has been recognized as a disease of great enough importance to give special time, consideration and study.

In our college, heretofore, it has been intimately connected with the study of genitourinary diseases, but Emory University, together with other large institutions throughout our country, has awakened to the fact that this disease is of such a nature as to warrant, and even demand, proper recognition, as its ramifications are such as to attack every tissue in the human organism and capable of complicating every other disease we are called upon to diagnose.

I desire to give an idea in as few words as possible of the work we are doing in our clinic and some of our methods used.

The dispensary is open four afternoons of each week for the reception of these patients, and it has been our aim not to be superficial in our examinations, but to be careful and thorough with the diagnosis, as well as treatment. The history blank we use contains outlines for a perfect physical examination, as well as the usual tests for obscure syphilitic lesions.

We have thought it best to separate the sexes, and, therefore, have the women on Monday and Wednesday afternoons, and the men Tuesday and Friday. The first two days mentioned are for the intramuscular injection of some of the insoluble salts of mercury (generally the salicylate) and the last two for the intravenous administrations of the arsenical preparations (salvarsan, diarsenol or arsenobenzol.)

We contend that the mercury is just as important as the intravenous injections of salvarsan, and insist that the patients can not, as a rule, have one, unless they will consent to the administration of the other.

To give some idea of the magnitude of our work, I might mention that during the months of October and November, 1917, 903 treatments were administered to patients admitted to the clinic. During these two months, we gave 347 doses of mercury and 241 doses of the arsenical preparations (diarsenol, arsenobenzol and salvarsan). This, of course, is not the full extent of our treatment, as many received internal administration of bichloride of mercury, iodide of potash, the protoiodide of mercury or reconstructive tonics during their rest period.

Our department of syphilis might be likened unto a pond into which flows a stream from each department of medicine and surgery. We have many patients transferred and some only referred for a certain course of treatment suggested by the physician sending them to us.

We have assistants acting as representatives of the several departments, and those from neurology and pediatrics I consider especially valuable, the first being of great assistance in our spinal work, and the latter in the handling of children.

I understand that in many of the large clinics, there exist to some extent, petty jealousies between the dermatologists and the syphilologists. In our work perfect harmony exists. The dermatologists, after diagnosing, refer patients to us for treatment, and I often find them of great service to me when it comes to the fine points of diagnosis in skin lesions.

I feel that this report will not be complete unless I mention the value we place in the methods we use in trying to educate the patients to some degree, at least, concerning the disease they are harboring. We make every effort to gain their confidence and cooperation. All of us know that many patients in our clinics discontinue treatments long before they are cured, hence the large number of severe tertiary cases that return years later. I am sure this occurs, in the great majority of cases, through ignorance on the part of the patients. We not only try to explain to each individual the necessity of long, systematic and thorough treatment, and the danger of being misled by the disappearance of external lesions, but we give to each patient a slip, printed in simple language, setting forth the nature of the disease, prophylaxis, and the necessity of thorough treatment.

To those who can not read and to the very ignorant, this information is read and explained by a student or assistant.

## SYPHILIS AND THE WAR

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THAT syphilis always increases both during war time and during the period of five years following war, both among soldiers and among the civil populace is a well recognized fact. One has only to turn to the article of Melville<sup>1</sup> to see how great this increase has been in the various Continental armies and in the American army. The present war has been no exception to this rule. Every writer has emphasized the great increase in the number of cases of lues, both in the army and among the female portion of the population, both the wives of the soldiers and the loose women. Before the war started the admissions for syphilis per 100,000 of the army were as follows: England (1908), 19.19; United States (1908), 28; Germany (1906), 4.7; Bavaria (1908), 3.6; Austria (1906), 19; Belgium (1906), 6.12; Italy (1902), 12.5. That these percentages have increased greatly may be proved by a brief consideration of the following facts: Pautrier<sup>2</sup> states that in 1916 there were 200,000 cases of acute syphilis along the French battle line alone, and Gaucher<sup>3</sup> reckons that in Paris the disease has increased 66.6%. Balzer<sup>4</sup> believes that up to February, 1915, the Germans had 30,000 fresh cases in their Belgian army alone. I have been told by unimpeachable authority that syphilis has also greatly increased in the Italian army and also among the wives of the soldiers.

It would naturally follow that if the troops became infected, a number of other persons would be put in immediate danger; that there have been a large number of extragenital chancres among the soldier associates seems to be proved by the statements of Cole<sup>5</sup> and Tullidge.<sup>6</sup> That syphilis has greatly increased among the prostitutes is commented upon by practically every writer on the subject. One of the saddest facts is that the soldier not infrequently returns home only to infect his wife, and that later we shall have a crop of congenital syphilitic children.



It has been found necessary not to debar men from the draft because of syphilis, unless the disease cause disability, such as would result from aortitis, serious bone disease, or lesions of the central nervous system. To this might well be added still another group; namely, those who have persistently recurring mucous patches, which, as we well know, are a grave source of danger. Of course, no man with active infectious lesions can safely be admitted to the training camps, but salvarsan treatment will speedily render such lesions innocuous.

In our own cantonments there have been but a comparatively small number of fresh cases of venereal disease, although many more than there should be. Here the infected men can and do receive satisfactory treatment from the onset; these men must not be discharged from duty because of their infection, if this were done there would unfortunately be many who would deliberately become infected in order that they might not have to go to the firing line, not knowing that the ultimate mortality from syphilis is greater than that of battle.

Troops upon the firing line with fresh or with contagious lesions of syphilis are usually removed to a hospital where they receive appropriate treatment, and are then returned, thanks to the more intensive ways in which salvarsan is now administered this is usually possible in at least six weeks.

France has her battle lines divided into twenty-one divisions, with a base hospital for syphilis and gonorrhea for each division. This is usually considered the best method of treating syphilis by those competent to understand the situation, and other nations are modeling their plans like the French.

Troops when upon furlough are apt either to acquire syphilis or to spread it, either to their own families or to women with whom they may have intercourse. How to control the spread of infection at this time is one of the most serious problems of the war, and one as yet unsolved.

When troops are discharged from the army, the same thing is apt to happen as during furlough, and for this some provision must be made.

Not only the trooper and his immediate associates are to suffer from the ravages of syphilis, but society at large as well, as has

often been pointed out, and society must protect itself against not only the spreading of the infection to the innocent, but also against the economic losses incident to a spread of this disease. To do this no half-way measures can be taken; the firmest and most thorough are the best.

Various nations have made various attempts to prevent the spread of syphilis in the army. The French commission, composed of Balzar, Beclere, Bourquelot, Gaucher, Grunbert, Hallopeau, Landouzy, Pierre Marie, Pinard, Pouchert, and Vaillard recommended the following measures:

1. Medical supervision of all tolerated houses of prostitution consisting of daily visits, and biweekly visits to all registered prostitutes.
2. Sanitary visits by the military authorities every fifteen days.
3. Medical supervision of all inhabitants of a region occupied by soldiers on their way to work.
4. Prohibition of street soliciting.
5. Police supervision of public houses.
6. Interdiction of women to the war zones, except those with permits.
7. Establishment of special hospitals for the treatment of venereal diseases for both military and civil cases.
8. Instruction of troops in reference to the dangers of venereal diseases.

In addition the French furnish a pamphlet to each of their soldiers, which reads as follows:<sup>7</sup>

#### SOLDIERS, BEWARE OF VENEREAL DISEASES

(1) The venereal diseases, especially gonorrhea and syphilis, gravely affect the health. It is the duty of a good citizen and soldier to conserve his health for the service of his country.

(2) Do not think that sexual continence is harmful. It conserves all the powers of the human body. It is quite apparent that it is the surest way of avoiding venereal disease.

(3) Friend! Have a care, for some day a venereal disease may be transmitted to your family, to your friends, and, especially, to your wife and children. Do not lose their love, esteem, and respect. Should you be honorable with your family? Would you have their love if you infected a sister or daughter?

(4) Beware of all females who solicit the passerby in the streets. You may well know that they are infected and that you risk contagion through them.

(5) Beware of their kisses, for the mouth of an infected person can give you syphilis, just as well as contact with their sexual organs. Do you know that venereal diseases are much more common now than in times of peace?

(6) If at any time, in weakness, you have allowed yourself to be tempted by these women, do not forget to use a "protector" of rubber. Also be careful to first oil your penis with some fatty substance, suet, oil or tallow, or, better still, with a disinfecting ointment containing 30 per cent of calomel. Do not touch either the mouth or sexual parts after sexual intercourse. Wash the penis and adjacent parts vigorously with soap and water and if it is possible with a solution of bichloride 1:1000. It is also best to urinate immediately after intercourse.

(7) If you have a discharge, you can be sure that you have a venereal disease and go immediately to the doctor and continue with him until you are cured. He will be your sole confidant and counsellor.

(8) It is also well to know that syphilis can be contracted in other ways than from a female, by contact with objects belonging to a person with syphilis such as cigarettes, pipes, glasses, forks, razors, napkins, handkerchiefs, etc. Beware of contact with persons whom you know have syphilis, men or women, as well as with objects which they may use.

(9) A man affected with a venereal disease should abstain from all sexual intercourse. He should wash his hands after having touched his sexual organs. In case of syphilis one should kiss neither parents nor friends. The table utensils and his laundry articles should be used by him alone. Otherwise he risks giving the disease to others and adding to his troubles as well as prejudicing himself to society and his country. If a complaint be lodged against him, the judicial procedures will be severe.

(10) In bawing of prostitutes you guard your health for the girl whom you will marry and for the mother of your children. You may be sure that, thereby, during the war you will keep intact your courage and strength for your country.

Goodwin<sup>8</sup> considers that conditions in the English army are fairly satisfactory and he attributes them to the following factors: Improved education of the troops, the provisions of games and recreations in the cantonments and the decrease in alcoholism. May<sup>9</sup> states that the use of female police has aided greatly in controlling women. The Royal Commission on Venereal Diseases<sup>10</sup> has recently issued an elaborate report, but one which to my mind is not sufficiently radical. It reports favorably on education, better diagnosis, and treatment, the suppression of quackery, and punishment for the willful communication of venereal diseases. As contrasted with the measures recently passed in Australia, and outlined elsewhere in this volume, it is decidedly weak. In Australia<sup>11</sup> it will be remembered that compulsory treatment by licensed practitioners is provided for.

The handling of the problem in Germany has recently been published in a special article in the *Journal of the American Medical Association*,<sup>12</sup> and I shall quote from this article. "The increased efforts for the control of the diseases have been extended, not only to the part of the population which is in military service, but also to the civilians both in the military districts and elsewhere. The German efforts have taken two directions: first, the Continental course of regulating prostitution and rendering it as little dangerous as possible, and, second, efforts to combat the venereal diseases directly.

"In military districts the most stringent regulation of prostitution has been effected, and outside of the military districts measures for the control of prostitution have been more rigorously enforced. Among German authorities, such as Neisser and Blaschko, there has been marked difference of opinion as to the sanitary value of regulation and examination of prostitutes. These measures are admitted by their advocates to be of only relatively small usefulness—certainly not of sufficient value to rekindle any hope of great benefit from them. German experts give the regulation of prostitution an entirely minor, if not, indeed, a negligible place among the measures for fighting the venereal diseases.

"In Germany, as elsewhere, great stress is being placed on diagnosis and treatment for combating venereal diseases. The insurance companies, under which so large a proportion of Germany's industrial population are being cared for, are furnishing general facilities for treatment of these diseases along the same lines that are being followed elsewhere. Government measures for providing universal opportunities are in process of establishment. \* \* \* \* It is recognized that the weak point in this plan of treatment outside of the armies in Germany is the lack of authority to compel patients to continue treatment until they are freed from infectious danger to others.

"The recommendations for combating venereal diseases of a committee appointed to study this question by the Medical Association of Munich were recently reviewed in *The Journal*.<sup>13</sup> This committee presented a report which proposes to remedy the failure of patients to pursue treatment by requiring compulsory treatment as long as there is need for it. The recommendations of the Munich

committee closely conform to the regulations which have been put in force in Western Australia. \* \* \* \* Patients must seek treatment immediately on the appearance of the venereal disease. Suspects may be examined by boards of health and compelled to take treatment. Checks are provided so that patients who fail voluntarily to continue treatment will be compelled to do so, and, as in the Australian act heavy penalties are provided for the failure of patients or physicians to live up to their responsibility under the plan. The recommendations of the Munich committee go still further, and urge stringent measures for complete notification of the venereal diseases; but they recommend that the records of such notifications be provided with all possible safeguards of secrecy. The recommendations of this committee go much further than the general sentiment of the German profession. German medical authorities are agreed on the value of providing opportunities for treatment, and appreciate the need for measures to compel the continuance of treatment; but apparently there is wide difference of opinion as to the desirability and practicability of notification of the venereal diseases.

“The German efforts differ from others we have considered in placing important emphasis on the value as a sanitary measure of the personal prophylaxis of syphilis. Every effort is made to see that personal prophylaxis is carried out in the armies, and it is also being utilized among the civilian population. Where previously the condom was under legal ban as a means of preventing conception, its use to prevent venereal infection is widely and frankly advocated. Calomel ointment and other medicinal preparations for preventing infection are being distributed to soldiers and the public, and leaflets are being furnished which describe the methods of use of these devices. Neisser took the position before the Deutsche Gesellschaft für Bekämpfung der Geschlechtskrankheiten at its meeting in 1915 that measures of personal prophylaxis were of essential importance in the fight against the venereal diseases.

“Much anxiety is being shown in Germany concerning the danger of the spread of the venereal diseases by soldiers after their discharge, and vigorous methods are proposed for combating this danger. Neisser and others have urged that every soldier, officers included, should at the end of the war be given a Wassermann test,

and an equally comprehensive plan is suggested for detecting gonorrhea among soldiers before their discharge. Blaschko's proposals, though less extreme, represent the last degree of radicalism when compared with anything of this sort that has ever been done before. He proposes, before discharge, examination of the men who have suffered during enlistment from venereal diseases; retention under military control of men with active cases until a cure is effected; transference to the insurance companies for observation, and, if necessity should arise, for treatment, of men who have had venereal diseases during the war, but in whom the disease is no longer active. Many have urged the continuance of the severe restrictive measures which have been instituted and proved valuable under military rule, such as severe penalties for intercourse when persons are affected with venereal diseases, and the suppression of quackery. There is the same insistence on the continuance of the thorough military measures for diagnosis and treatment."

In the United States no systematic attempt has been made to decrease the amount of syphilis in either the army or the navy, and the result has been an appalling number of cases, the highest in any country. This is largely due to the fact that the services have not been taken out of politics and that various enthusiasts have been able to try beautiful moral schemes that have not worked well in practice. Various enthusiastic and capable surgeons have done good work in limited fields, but as a whole the preventive work has not been good.

Cole is authority for the statement that when our regular army was on the Mexican border there were supervised prostitutes who lived with the army, being made a part of the regiment as it were. The prohibition of alcohol in the neighborhood of the camps and training stations is unquestionably of extreme value. Riggs<sup>14</sup> and Cole both report that the closing of the houses of prostitution have a beneficial effect.

The Surgeon-General's office has authorized a statement<sup>15</sup> on the social hygiene program of the war department in relation to other agencies. So far the administrative measures may be grouped under five headings:

1. The army medical department will endeavor to instruct the men in the dangers of venereal disease, by talks, exhibits, pam-

phlets, etc. There will be prophylactic stations for lessening the danger of infection after exposure. Venereal diseases will be diagnosed early and effectively treated. Penalties will be imposed upon those men who persist in exposing themselves. Epidemiologic studies will be made.

2. The United States Public Health Service will promote public opinion in regard to social hygiene. It will survey and standardize hospital and clinical facilities for the treatment of venereal diseases. It will cooperate with private practitioners in lessening the dangers of dissemination. It will extend its laboratory, clinical, and advisory services for venereal diseases in civil communities.

3. The civil authorities are to enforce the laws against prostitution and use of alcohol, establish suitable facilities for the proper treatment of venereal diseases, provide recreation for the population, educate and protect women and girls.

4. The Commission on Training Camp Activities is to enforce certain law measures, namely, elimination of commercial prostitution in the cantonment zones, repress clandestine prostitution, control sale of alcohol, combat the use of drugs and gambling. Also it is to provide recreation for the troops.

5. There are many useful opportunities for various nonofficial volunteer agencies. A small number of such agencies can be used as clearing houses for the work of all of them.

To sum up the means of prophylaxis and their relative values we may say the following:

1. Actively infectious cases of syphilis should not be admitted to training camps or other military duties until the lesions are sterilized: patients who have repeatedly suffered from mucous patches despite radical treatment should not be admitted at all.

2. Every possible means of recreation and amusement is to be encouraged: the Y. M. C. A. is doing good work that must be encouraged in every possible way.

3. The sale of all strong alcoholic beverages, and probably of beer and light wines as well, should be forbidden around cantonments and near the front. It is a well recognized fact that many cases of syphilis are contracted while the man is under the influence of alcohol.

4. Street soliciting by women must be absolutely stopped.

5. Only women with permits should be admitted to all camps.

6. Inasmuch as we must look matters squarely in the face and recognize that a very considerable number of men will insist upon sexual indulgences, available women should be carefully looked after. It is extremely questionable whether we should follow the example of some of the Allies and have regularly licensed prostitutes, for this is bad morally and also, as Jolivet<sup>16</sup> has shown, far from safe; for supervised women can apparently disseminate venereal diseases just as readily as can clandestine prostitutes, and in addition the man feels that he is safe, and does not attempt to avoid infection. It would probably be well to have every soldier compelled to tell where he acquired his trouble and then put that woman under legal restraint, including treatment. In this work women police could be of great help. In addition any diseased woman who had intercourse should be liable to imprisonment, a fine would not suffice.

7. It is probable that those men who persist in sexual intercourse should be instructed in the use of condoms or urethral injections and mercurial ointments after intercourse. At the same time it should be remembered that Holcomb<sup>17</sup> has found that the latter means is not always efficacious. Yet other good observers feel that good results have been obtained by such means.

8. All troops should be educated in the dangers of venereal disease: this can be done by personal talks, lectures, lantern slides, etc.

9. Troops should not be permanently removed from the firing lines because of syphilis, they should only be removed to receive treatment during the early stages, or when a late infection becomes active. To remove troops for venereal infections would be to encourage them to acquire such infections.

10. Treatment must be prompt and efficacious.

11. Any person who willfully transmits syphilis or gonorrhea should be subject to severe penalties.

12. Every soldier, officers included, should be thoroughly examined upon being mustered out of the service, or upon being sent home on a furlough; this should include a Wassermann examination. If diseased, he should be required to continue treatment until cured.

13. In reference to syphilis among the civil population, there



should be national control and not state control or no control at all, of the situation: it is only through one broad and strong policy that the necessary results can be accomplished. The West Australia laws could well be used as models.

Cole<sup>18</sup> well summarizes the methods of treatment that have been advocated in various countries. Although such an authority as Neisser<sup>19</sup> has recommended the ambulatory treatment of all cases of syphilis, still the weight of evidence is much against him, and it is now pretty well agreed that all early or infectious cases should be sent to a special hospital where they may secure appropriate treatment. As has already been pointed out, France has her battle lines divided into twenty-one divisions,<sup>2</sup> with a base hospital for venereal diseases located behind each. The personnel must consist of a head, and at least one assistant for syphilis and one for urologic cases. Either the director or the syphilographer must be well versed in dermatology, because many skin diseases are so frequently mistaken for syphilis and vice versa. Pautrier has pointed this out very clearly. In addition there must be a dentist, as syphilitics who are to have intensive mercurial treatment need to have their mouths in the best possible condition. In each hospital there must be a laboratory where Wassermanns can be done and also dark-field examinations. Personally, I fail to see the need for animal experimentation in connection with this war work, although many authorities consider it necessary. If possible, there should be an x-ray outfit so that bone and aortic lesions could be early recognized. Certainly there should be a good general clinician attached so that visceral syphilis could be recognized. In regard to nervous syphilis, it is probable that there should be one special hospital to which such cases should be sent: it is doubtful if each of the venereal hospitals could find men competent to give intraspinal treatment.

In the hospitals it is essential to give the most rapid treatment possible. Our own army board consisting of Drs. Pusey, Pollitzer, Wende, Hagner and Morton<sup>20</sup> recommend that salvarsan be given at five-day intervals. Personally, I have been using salvarsan at three-day intervals ever since hearing Pollitzer's paper.<sup>21</sup> Pollitzer, it will be remembered, recommended that three doses of salvarsan be administered in three days, followed by a course of mercurial injections. I should strongly urge that five to six salvarsans be given,

at three-day intervals if the patients will tolerate them, otherwise as close together as possible. This can be followed by a course of mercurial injections, some of which could probably be given after the patient had been returned to the front.

Regarding the technic of administration, but little need be said, for it should be the same standard that is recognized the world over; that is, dissolving the salvarsan in water, neutralizing, and then diluting so that each tenth of a gram is in about 15 c.c. of water, the water must be freshly distilled, and either autoclaved or twice boiled. There has been considerable discussion as to the advisability of giving salvarsan in more concentrated solutions and administering with a large syringe: this I do not believe to be advisable as a routine procedure, as concentrated solutions have been shown to have an injurious effect upon the vessel wall. Nor do I believe that neo-salvarsan should be used, even though it is easier to administer, for both laboratory and clinical work have plainly shown that it is not so effective as is salvarsan.

In conclusion, it may be well to point out the various recommendations which our advisory committee has made. First, it points out the necessity of keeping complete case records, recommending the present army register for that purpose. Second, it wisely points out the necessity of making an early diagnosis, especially insisting upon the use of dark-field illumination in all cases of venereal sores: in addition it recommends the obtaining of fluid from enlarged lymph nodes by aspiration in all doubtful cases. It also believes that the Wassermann should be done in all cases. Third, it is not enthusiastic about the excision of the chancre, although recommending it in a half-hearted way; it appears to prefer a calomel ointment, which is in harmony with the generally accepted ideas. Fourth, it believes in both salvarsan and mercurial treatment, both strongly pushed. As regards the administration of salvarsan it recommends that the first three doses be given at intervals of five days, and the remaining five at weekly intervals, this to be combined with either mercurial injections or inunctions. It also points out that such patients should be watched for a year with monthly Wassermann tests, and promptly treated should any evidences of a positive reaction become manifest. "In all cases seen after the Wassermann test has become positive the first course of treatment should be followed

by a second after six or eight weeks' rest. And it is safest to give at least a third similar course after an interval of two months even in the most promising of cases." The discussion of the technic of administration requires no special comment, as it is standard. In regard to mercury, it states that a mercurial course should consist of six to eight weekly injections of an insoluble salt, or from thirty-five to forty-five inunctions. In late cases where there are no serious lesions, it recommends mercury and potassium iodide until a symptomatic cure takes place. Unfortunately it does not recommend that such cases should receive sufficient treatment to render the Wassermann negative, a procedure which many of us believe to be imperative.

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## EFFECT OF VENEREAL DISEASES ON INFANT MORTALITY

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THE two diseases with which we are concerned in this paper are syphilis and gonorrhea. It is difficult to get accurate information about the actual effects of these diseases in causing infant deaths. In the case of gonorrhea the effect of the disease in the actual causation of the death of the infant is almost negligible. In the case of syphilis, the actual number of deaths from the disease itself seems small compared with the deaths from respiratory disease or from disease of the intestinal tract. Tuberculosis even is responsible for a much larger number of infant deaths than congenital syphilis. Why, then, are congenital syphilis and gonorrhea diseases to be taken seriously in their relation to infant mortality?

In the discussion of this subject the term *infant mortality* will receive a broad application. It will include actual deaths, the deaths of children in the uterus, the effects of these diseases upon birth rate by preventing conception, and the deforming effects of these diseases.

Gonorrhea is of importance because of its effect in preventing conception. Its almost invariable mode of transmission is by sexual contact. In women it sets up an inflammation in the vagina or cervix. This inflammation may spread to the ovaries, the tubes, or the inner surface of the uterus. One or all of these parts may share in the inflammation. The ultimate result is to make impossible the giving birth to a child. In the case of the male, the disease may cause inflammation of the testicles or of the organs which transport the spermatazoa from the testicles. In either case the male is incapable of transmitting to the female the germ which must fertilize the ovum.

This disease, as you all know, is widespread. It is, however, impossible to determine what percentage of the males or females who have the disease in its local form are rendered sterile as a result of the complications just mentioned. It has been estimated that from 30 to 50 per cent of all women who have the local disease in the

vagina are subsequently rendered sterile by it.<sup>1</sup> Even assuming that these figures are exaggerated, the effect on birth rate is of great significance. Its bearing upon the renewal of the population after the war for all nations involved is important. The disease is regarded far too lightly. If the soldiers at the front and the married or unmarried women at home or elsewhere clearly understood the significance of gonorrhea in preventing conception, the disease might be taken more seriously.

An infant born of a mother whose vagina is the seat of an acute gonorrheal infection is submitted to the hazard of a disease called gonorrheal ophthalmia—or gonorrhea of the eye.<sup>2</sup> About 70 per cent of all cases of ophthalmia of the newborn is due to gonorrhea, and 25 per cent of all cases of blindness is attributed to gonorrheal infection. This infection is picked up as the infant passes through the vagina in the birth process. It is, therefore, in causing blindness that gonorrhea is of importance in infancy. It is one of the deforming effects of the disease which are included under the broader interpretation of infant mortality.

Syphilis on the other hand, has an intimate connection with infant deaths. As an agent in the actual destruction of infant lives its importance is far reaching. The figures recording the actual deaths from congenital syphilis may seem small. But it must be remembered that the disease begins its ravages in the fetus and that two individuals are particularly concerned—the mother and the child.

The mode of transmission of the disease is clear if the cause is understood. Syphilis is the result of an infection by a minute organism called the spirochete pallida. If the male has a local sore which has in it these organisms and if he has intercourse, these minute organisms are transferred to the female. A local sore results in the female organs as a result of the growth of these organisms. From this local sore the organisms find their way through the tissues into the blood stream. If the mother becomes pregnant, the spirochetes are transported by her blood into the blood stream through the placental circulation of the fetus, and are disseminated throughout its tissues. It, therefore, becomes clear that the mother of every syphilitic child is herself syphilitic.

The disease may also be conveyed to the fetus from the infected

mother through the ovum. This mode of transmission presupposes again a syphilitic mother.

Whether or not the father can transmit the organism directly through the semen without the mother's being diseased is a matter of dispute. The important fact is that syphilis probably in every instance is transmitted to the infant directly from the mother. If the fetus has received from the mother into its circulation the organism of syphilis, the result will be either the death of the fetus in the uterus or the birth of a syphilitic child.

It would be of interest to know the actual number of syphilitic pregnancies each year. It is impossible, however, to secure any accurate statistics. If stillbirths and miscarriages are included in an estimate of the incidence of congenital syphilis the number of actual cases is much larger than the present statistics show. Another difficulty in arriving at an accurate estimate of the effects of syphilis is the establishment of the relation of syphilis to stillbirths. Statements have been made that 50 per cent of all stillbirths are due to syphilis. This is probably an exaggeration, but is instructive in showing the need of more careful investigation into the relation of syphilis to stillbirths and miscarriages. A personal communication from Dr. Jacob Sobel of the New York City Health Department, Division of Baby Welfare, bears directly on this subject. He writes:

"An analysis of the stillbirth certificates recorded with the department would not give any accurate information, since it is well known that in a large number of instances the cause of the stillbirth is not recorded as due to syphilis when such is the case, for obvious reasons. Similarly, many cases of deaths during the first month of life, which are due to syphilis, are ascribed to other causes.

"The whole subject of stillbirths is one that offers a fertile field for investigation. Dr. Thomas has requested that a special study be made along these lines, and postmortem examinations, under the supervision of Dr. Norris, be performed at Bellevue Hospital. The names of several inspectors have been submitted, and the work will probably be taken up in the immediate future.

"The question of stillbirths and premature births is a broader one than that of syphilis only; alcoholism, syphilis, retroflexion, diseased adnexa and uteri, general constitutional diseases, toxemias, (pregnancy, plumbism, etc.), placental degeneration, and other factors, will have to be closely studied. The whole subject of syphilis

in relation to stillbirths and infant mortality is one in which we feel morally certain that this disease is a decided contributing factor in the direct and indirect causes of infant mortality, and yet it is one in which it is almost impossible to 'back up' our convictions by figures."

In order to make concrete the general statements regarding the effects of syphilis as a cause of stillbirths, Table I is instructive. The figures record the results of the pregnancies of 53 syphilitic women attended at the Tarnier Clinic from Jan. 1, 1915, to Aug. 31, 1916:<sup>3</sup>

TABLE I

	LAST PREGNANCY	PREVIOUS PREGNANCY
1. <i>Pregnancy posterior to syphilis infection</i>		
Miscarriage	3	15
Macerated infants or stillborn	20	18
Exencephaly	1	0
Infants dead before mothers left the clinic	3	0
Infants dead before first year	0	10
Infants living	15	5
2. <i>Pregnancy antedates the syphilitic infection</i>		
Living infants (infection of mother surely or very probably during the pregnancy)	9	0
Stillbirths (infection of mother during pregnancy)	2	0
Living infants (born after a series of miscarriages or stillbirths)	0	11
Infants born dead (mother albuminuric, having a series of miscarriages and stillbirths)	0	5
History of child unknown	0	1

The above table shows that in those pregnancies which are posterior to the syphilitic infection there were 56 stillbirths, miscarriages and macerated infants in 90 pregnancies, or 62 per cent. The term posterior is used to indicate a syphilitic infection of the mother antedating her child bearing period. These statistics are not cited with a view to indicate that the pregnancies of syphilitic mothers result in over 50 per cent of stillbirths. These figures, however, are illustrative of the possible effects of syphilis in a series of mothers who were under careful observation, and who for the most part had received antisyphilitic treatment.

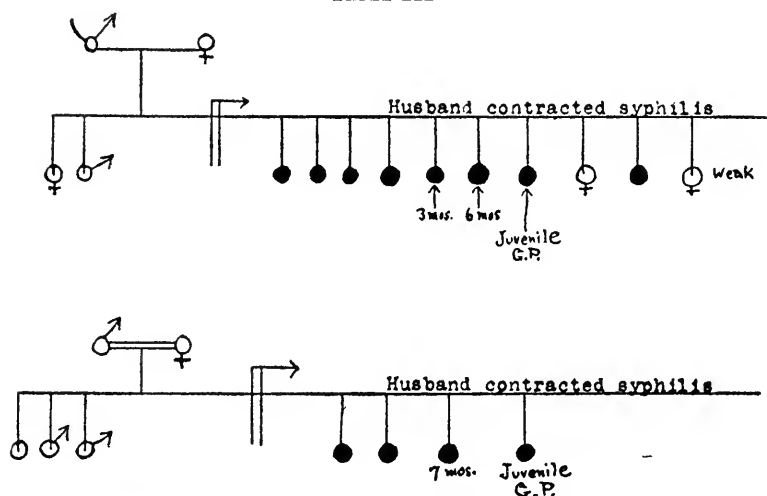
The records of the Babies' Hospital, New York City, give the following statistics on the frequency of stillbirths and miscarriages in syphilitic families.

TABLE II

Cases of congenital syphilis	193
Total number of pregnancies in the families of the 193 syphilitics	427
Stillbirths and miscarriages	123
Percentage of stillbirths and miscarriages of the total number of pregnancies	22.4

The 193 cases of congenital syphilis represent the number of infants with this disease in a total of 12,180 admissions to the hospital. The figures for stillbirths and miscarriages show a striking contrast to those quoted from Tarnier's Clinic. They are given here to indicate the difficulty that is presented in getting accurate data on this point. They are sufficient to indicate that the waste of life in stillbirths resulting from syphilitic infection is of serious significance. For every case of congenital syphilis there is a toll of stillbirths, miscarriages, and premature infants representing an important loss to the nation in relation to the increase of birth rate. It

TABLE III\*



- = Miscarriage, stillborn or died in early infancy
- ♂ = Syphilitic
- ♂ = Male
- ♀ = Female

\*Mott: Royal Commission on Venereal Diseases, Final Report, 1916, 30.



must be remembered that in many instances a series of miscarriages and stillbirths have paved the way for the production of a living child, which child begins its infancy in most cases with syphilis.

The diagrams shown in Table III will serve to illustrate the effect of syphilis on pregnancy in two families. These are not typical instances, but, on the other hand, they are not exceptional.

In order to make more generally available further facts bearing on the relation of syphilis to stillbirths and miscarriages, the following tables are introduced:\*

TABLE IV

FAMILIES OF 34 SYPHILITIC MOTHERS (DR. MOTT)

Mothers	Pregnancies	Premature births, stillbirths and deaths in early infancy	Children seriously diseased	Children apparently healthy
34	175	104	41	30

TABLE V

RECORDS OF 21 FAMILIES WITH SYPHILITIC HISTORIES (DR. KERR LOVE)

Families	Pregnancies	Miscarriages and stillbirths	Deaths in infancy	Children alive but deaf or deaf and blind
21	172	32	45	31

TABLE VI

RECORDS OF 150 FAMILIES IN EACH OF WHICH ONE OR MORE CHILDREN PRESENTED DEFINITE SIGNS OF INHERITED SYPHILIS (MR. BISHOP HARMAN)

Families	Pregnancies	Miscarriages and stillbirths	Infant deaths	Children alive but diseased	Children alive and healthy
150	1001	172	229	390	210

TABLE VII

RECORDS OF 150 POOR FAMILIES IN LONDON—DEFINITELY KNOWN CASES OF SYPHILIS EXCLUDED, BUT NO SPECIAL STEPS TAKEN TO ASCERTAIN PRESENCE OF SYPHILIS

Families	Pregnancies	Miscarriages and stillbirths	Infant deaths	Healthy children
150	826	78	94	634
Expressed per 1000 pregnancies.	1000	94	114	792

Tables VI and VII offer an instructive comparison. Table 3 shows a record of 172 miscarriages and stillbirths in 1001 pregnancies which occurred in syphilitic families. Table VII records 78 miscarriages and stillbirths in 826 pregnancies (or 94 in 1000) which

occurred in families that were in all probability nonsyphilitic. The greater frequency of stillbirths and miscarriages in syphilitic families is clearly indicated in these tables.

The following statement<sup>5</sup> is introduced to give an idea of the estimated loss of life resulting from stillbirths, miscarriages and premature births. It would be of great interest to know what part of this total loss could be ascribed to syphilis.

	1910	Loss to population in 1911
Estimated abortions, premature labors, and stillbirths in married and unmarried women	98,680	96,925

There are students of this subject who say that syphilis would account for one-half of this loss. That estimate is probably too large. At the same time the waste from syphilis alone is sufficiently great to make important inroads into birth rate.

The usual progression in the events of pregnancy in syphilitic families is one or more stillbirths or miscarriages and finally a living child. This child may be premature or carried to term, but the product is the same—a syphilitic offspring. If the child is premature, its hold on life is so much the slighter.

It is again difficult to obtain accurate statistics regarding the number of infantile deaths from syphilis, and further to discover what percentage of infants with syphilis survive. The figures of different observers show considerable variations particularly regarding those that survive.

The Foundling Hospital at Moscow reports that 70 per cent of their syphilitic children die in the first six months. Fournier states that in private practice 60 per cent of syphilitic infants die, and in hospital practice 85 per cent. Presumably these cases were untreated. Etienne accounts for 95 per cent of untreated cases and 10 per cent of treated cases.<sup>6</sup> In 193 cases of congenital syphilis in the Babies' Hospitals, New York, there were 26 deaths from the uncomplicated disease, or 13.4 per cent. All these cases received treatment except the few who died before treatment could be given a trial. There were 35 deaths (18.6 per cent) of infants having complications, such as bronchopneumonia, acute diarrhea, marasmus, and acute nephritis, etc. Those cases also received treatment. The total percentage of deaths in cases with and without complications was

32 per cent. It should be noted that all of these patients died in their first admission to the hospital.

Dr. Kerr Love's figures in Table V show 45 deaths in 140 pregnancies, and Mr. Bishop Harman's figures (Table VI) give 229 deaths in 889 pregnancies. No statement is made as to whether or not these infants received treatment. The figures in Table I reported from the Tarnier Clinic show that in a total of 118 pregnancies, 40 (or 34 per cent) living children were taken home by their mothers. An analysis of the table recording the conceptions which definitely took place after the syphilitic infection shows that only 22 per cent were taken home alive—20 live infants in 90 pregnancies!

The above figures suffice to show that the percentage of deaths of congenital syphilis in relation to the total number of cases of the disease is high. After all, statistics convey scant information about the seriousness of the disease. They contain no record of the mental suffering of the mother who has to rear a syphilitic child and whose anguish of mind is intensified by the knowledge that she has the disease herself. Statistics do not tell anything of the burden of caring for the syphilitic infant, requiring as it does constant and unremitting treatment for a period of a year or more, and there are no records of the mental state of the mother in facing the prospect of future pregnancies.

A review of the total deaths from congenital syphilis conveys inadequate information of the peril of the disease. In comparison with the deaths from other causes, the totals are small. The following reports are introduced here to make the statistical material more readily available.

TABLE VIII

TOTAL DEATHS ENGLAND AND WALES, 1915 <sup>7</sup>	ALL AGES	UNDER 1 YEAR
Male	1090	676
Female	795	493
	1885	1169
U. S. STATISTICS, 1915	MALE	FEMALE
Total	3715	2104
Under 1 year	1118	904
Under 5 years	1228	1021

The fact of importance in the above table is that, of the deaths from syphilis, all ages (England and Wales), 62 per cent are under 1 year, and that 38.6 per cent (U. S. Statistics) are under 5 years.

Presumably most of the cases under 5 years are congenital syphilis. These figures emphasize the point that syphilis causes the death of infants in greater numbers than it causes the deaths of adults, and in practically every instance an infant who dies of syphilis has acquired the disease from its parents. This I believe will hold true for children under 5 years of age. In other words, syphilis has significance as an adult disease because of its effect upon offsprings. It is for this reason that the disease has been called "a national peril."

The following table (Table IX) from the Registrar General's report for 1915 gives the proportion of deaths under one year from syphilis to 1,000 births for England and Wales.

TABLE IX	
CONGENITAL SYPHILIS	
PROPORTION OF DEATHS TO 1000 BIRTHS ENGLAND AND WALES <sup>7</sup>	
1891-1900	1.46
1901-1910	1.25
1911-1915	1.42
PROPORTION OF DEATHS TO 1000 BIRTHS ENGLAND AND WALES, 1915	
Male	1.63
Female	1.23
Average	1.44

Table X, from the Department of Health, New York City, will serve as a comparison with the above:

TABLE X	
PROPORTION OF DEATHS TO 1000 BIRTHS, NEW YORK CITY <sup>8</sup>	
1891-1900	1.62
1901-1910	1.85
1911-1915	1.94
1916-	1.39

The ratio of deaths to 1000 births are approximately alike in the English and New York City reports—three children die of syphilis in every 2000 births.

No reference has thus far been made of the after effects of congenital syphilis in those cases that survive. These infants at different periods in their lives may show the deforming effects of the disease in various ways. The disease may assail the bony tissue, causing deformities in the bones of the legs, or it may invade the

bones of the nose, resulting in such complete destruction as to obliterate the bridge of the nose. It may invade the tissues of the throat, resulting in destruction of tissue with resulting hoarseness and modification of the voice. It may work its destructive effects in the tissues of the central nervous system. In the last instance the effects may not be manifest until youth or middle age. The ultimate product of the effect in the central nervous system is imbecility or paralysis, or both combined. The disease may invade the eye, resulting in total or partial blindness or in such destruction of its tissues as to cause unsightly scarring of the surface of the eye. The disease may manifest itself by partial or total deafness. This result may not appear until puberty or after. It is needless to enumerate the further effects of the disease. It is only necessary to remember that the organism which causes the disease may lodge in any of the tissues of the body and there carry on its destructive effects.

If all infants with congenital syphilis had received appropriate treatment, the disastrous results which have just been mentioned would be largely eliminated. It is true also that the mortality of the disease would be greatly diminished. But it must be remembered that the nature of the disease is such that it requires constant and regular treatment over a considerable period (between two and three years at least) to make certain of the elimination of the disease. There is only a small percentage of parents who are willing to give up their time in carrying out such treatment, and it is on account of the prolonged nature of the treatment that the eradication of the disease is difficult.

If the organism of syphilis was only large enough so that it could be seen with the naked eye instead of by the high powers of the microscope, the disease would be regarded with more respect. An individual would avoid with disgust a contagion which resulted in flooding his blood stream with maggots, but in the majority of instances, he will take a chance, without fear, of submitting his tissues to an invasion of spirochetes.

A study of the above material in relation to the conditions created by the nations at war will be of profit. Unfortunately it is impossible to state in definite figures the toll of miscarriages and stillbirths for a definite number of syphilitic soldiers. But every one must admit

that a "national peril" exists in the form of reduction of birth rate if there is a considerable number of soldiers infected with the disease. A carefully organized propagandum is under way in all the nations at war to encourage child-bearing. It is necessary, therefore, to check the spread of syphilis among the soldiers if they are to do their share in renewing the races after the war. The following figures need no elucidation in this matter of race destruction and race renewal. Pautrier<sup>9</sup> estimates that there are 200,000 soldiers infected with syphilis in the French army. If each of these cases accounts for only two stillbirths the infection will account for 400,000 births. Table XI shows a number of living births, birth rate per 1000 population, and infant mortality in Paris from 1910 to and including the first five months of 1917.

TABLE XI<sup>10</sup>

YEAR	NO. LIVING BIRTHS	BIRTH RATE PER 1000 POPULATION	INFANT MORTALITY
1910	55,320	18.1	98
1911	55,521	17.2	117
1912	55,257	17	103
1913	48,746	17.1	99
1914			
1915	30,537	10.5	124.5
1916	27,995	9.7*	102
5 months			
1917	10,096	8.4*	124.6

\*Population of 1911 census.

An examination of the wastage of life in hereditary syphilis and of the falling birth rate in Paris can lead to but one conclusion, that syphilis is a national peril.

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## ADEQUATE TREATMENT FOR SYPHILIS\*

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IT might well be said that this war is going to bring venereal diseases into its own, for there never was a time when such an opportunity presented itself for those interested to accomplish so much. When the federal government, through official channels, declares that control of venereal disease is just about the army's greatest problem, people begin to realize in a general way the havoc wrought by syphilis and gonorrhea and to listen to ways and means to control this scourge. Medical men, as well as laity, needed this stimulus; and it is to be hoped that the medical profession will seize this opportunity and make the most of it.

I have had ample opportunity in my clinic to observe many patients who had been poorly and inefficiently treated. More recently, since undertaking the organization of the work of control of venereal diseases in the State of California, this fault has been still more emphasized.

When we realize that for several weeks the rate of venereal disease in the new national draft army has been nearly three times that of the regular army, we should understand just how important it is that the treatment of venereal diseases among civilians be bettered. It seems, therefore, quite pertinent to call attention to some mistakes made by the medical profession in general and to suggest a sort of standard of treatment which might be followed in the average case of syphilis. An attempt has been made to outline a treatment which represents in a general way the concensus of opinion of recognized syphilologists. It must, of course, be understood that ideal modern treatment is individualized as much as possible and that general rules can not be applied to exceptional cases. Emphasis

\*This paper has been embodied in a pamphlet to be issued by the Bureau of Venereal Diseases of the California State Board of Health and copies may be had by writing the Bureau at 512 Underwood Bldg., San Francisco.

should be placed upon the following fundamentals as accepted by practically all syphilologists.

Salvarsan\* or equivalents should be given to all cases of syphilis unless there are contraindications. Contraindications are for the most part only relative; that is, salvarsan can be given to practically every case if given cautiously and in sufficiently small doses. Cases complicated by severe nephritis, aneurysm, aortitis, myocarditis, pulmonary tuberculosis, diabetes, or cases of syphilis involving cerebral thrombosis, tabes dorsalis, paresis, nephritis, iritis, or meningitis, require caution. Mercury should be given by intramuscular injection or inunction. Its internal administration, except for short periods between courses of more intensive treatment, can not be accepted as of any value in the cure of syphilis. It is regarded as necessary that all cases of syphilis developed to the point of a positive Wassermann, require never less than two, and in many cases three years of active treatment. Care should be exercised in making a diagnosis. Every initial lesion should be diagnosed by the microscope in order that there may be no doubt later as to the correctness of the diagnosis. Skin lesions should not be diagnosed syphilis because of a positive Wassermann, neither should syphilis be denied because of a negative blood test. In general, the Wassermann should be taken into consideration with the rest of the clinical symptoms. Only occasionally does the diagnosis depend entirely upon the blood test, and when it does, it is suggested that repeated tests be made before treatment is instituted.

It should be remembered that many unpleasant and serious neuro-recurrences have followed the administration of single doses of salvarsan, or its equivalents. If salvarsan is to be administered at all, a series of at least three doses should be given. The interval between is from one to two weeks. Usually salvarsan will more quickly clear up lesions than mercury. It is especially valuable in healing mucous membrane lesions, moist lesions around the genitals, and all ulcerative lesions and eye lesions such as iritis and interstitial keratitis. For intramuscular injection, the salicylate of mercury is most commonly used, a suspension in paraffin or olive oil. For inunction the official Unguentum Hydrargyrum Dilutum may

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\*The word "salvarsan" is used throughout the paper to denote any of the recognized arsenicals such as salvarsan, neosalvarsan, diarsenol, neodiarsenol, and arsenobenzol.



be used in 4 gram doses, or a 50 per cent calomel ointment in lanolin and benzoated lard; the latter has the advantage of cleanliness. It must be remembered that while iodide of potassium frequently has a marked influence on certain lesions of syphilis, it does nothing toward eradicating the germ from the system.

Especially to be condemned is the practice, which is common in many localities, of those engaged in special lines who make it a rule to treat a patient until the lesions affecting various special organs are cleared up and then allowing the patient to pass from observation with no arrangements for continued routine treatment. Either the specialist should at once have a competent syphilologist institute systematic treatment, or should see to it that his patient passes into such a one's hands so soon as the particular symptoms have cleared up. The California State Board of Health has recently passed regulations requiring that clinics and private practitioners instruct their patients concerning the seriousness, infectiousness, and necessity of long-continued treatment of syphilis, and distribute literature\* including this information. One practice is especially to be condemned—that of attempting to connive with husband or wife to effect the treatment of one without the other's knowledge. It is obviously impossible to hope to give anyone sufficient or adequate treatment under such conditions. The vague terms "touch of syphilis," "a little blood disorder," and the like, can not be too strongly condemned. In the past it has been quite customary to put the obligation of continuing treatment upon the patient; the amount of late syphilis demonstrates how unsuccessful this has been.

It is to be hoped now that the medical profession will realize that practically speaking, we are dealing with a preventable disease, and that medical men must accept the obligation of doing their large part in stamping it out. The intelligent education of all patients is an extremely important part of this work.

#### TREATMENT

*Cases of Early Primary Syphilis with a Negative Wassermann and no Glandular Involvement.*—Under this heading may be considered patients having present an initial lesion with positive spirochete

\*Pamphlet "Syphilis and Gonorrhea" may be obtained by application to Bureau of Venereal Diseases, 512 Underwood Building, San Francisco.

findings, no glandular involvement, and a negative Wassermann. These are fit subjects upon which to attempt the following abortive treatment.

It will be of advantage to excise the lesion, if such a course is practicable. At least six doses of salvarsan should be given at weekly intervals. Not less than a six weeks' course of mercury injections or inunctions should be given, and this followed by another six doses of salvarsan. In such a case, if the Wassermann, done at frequent intervals, and clinical symptoms remain negative, the possibility of cure is good.

*Cases with Initial Lesion, Glandular Involvement and Positive Wassermann.*—Such cases must be considered in exactly the same light as an established secondary syphilis, and require an equal amount of treatment. Unless this is done, experience in large clinics has demonstrated a very large percentage of later recurrences.

*Cases of Established Secondary Syphilis.*—Under this heading may be considered cases with infection dating back from six to eight weeks to several years, having any of the following symptoms: roseola, muscular, papular, or pustular eruptions, mucous patches, gummata, periostitis, etc., and a positive Wassermann. The attending physician must make a choice as to whether to use salvarsan or mercury first. If the patient has infectious lesions, it is urged that salvarsan be given at once to quickly heal these.

*First Year.*—During the first year in such cases, not less than eight or ten doses of salvarsan should be given, and either in combination with or between the series of salvarsan injections, not less than three courses of mercury injections or inunctions should be given. Each course of mercury injections or inunctions should last from six to eight weeks.

*Second Year.*—(A.) In the second year, if the Wassermann remains positive, or recurrence of lesions takes place, repetition of the first year's treatment is suggested.

*Second Year.*—(B.) If the Wassermann has become negative, and remains negative, and there has been no recurrence of any symptoms, not less than six doses of salvarsan should be given, preferably in two series, and at least two courses of mercury injections or inunctions should be given.

*Third Year.*—For cases coming under the second year A, if the

Wassermann has been positive, or there has been recurrence of lesions in the second year, at least as much treatment as is suggested for second year *B* should be repeated. If the Wassermann has remained negative, and there has been no recurrence from the first year, a large percentage of cases will likely remain well, and may pass into the period of observation. In the case of patients having a positive Wassermann, or recurrence of symptoms after completing the two years' treatment, a competent syphilologist should be consulted or the patient referred to such a one that adequate individual treatment may be given.

*Early or Late Nerve Involvement.*—Usually in such cases the treatment is too individualized to be covered by general rules. It may be said, however, that such cases require more treatment, perhaps double the number of doses of salvarsan, and three or four years treatment, instead of two or three years.

*Tabes and Paresis.*—Modern treatment of tabes has in many cases produced brilliant results. The question of intravenous and intraspinal medication is more or less unsettled, but it may be said in general that the results depend upon salvarsan medication, and that a great many more doses are needed than in other cases (as high as twenty or thirty). It is frequently necessary in these cases not only to start with small doses, but to continue with them. It is suggested with this type of case that either a competent syphilologist be called in consultation, or the patient be referred to one. Results in paresis are questionable. In some cases conditions have been alleviated by intravenous or intraspinal treatment. As with tabes, the treatment must be considered in an individual way, and it is suggested that a competent syphilologist or neurologist be consulted.

*Cases of Hereditary or Congenital Syphilis.*—In general, these patients require longer treatment than is necessary for earlier cases of acquired syphilis. There are at least two reasons for this. First, these young patients have not the amount of inherent resistance to disease; and second, they can not, as a rule, stand such intensive treatment as can be given to an adult. In general, the same treatment should be given as to an established case of acquired syphilis; not less than twelve or fifteen doses of salvarsan (necessarily of proportionately smaller dosage) and at least five or six courses of mercury inunctions. Injections in most cases are not practicable.

Internal treatment is likewise to be condemned in these patients. At least 80 per cent of such of these patients as show lesions will have iritis or keratitis and better and quicker results are to be expected from graduated doses of salvarsan given in weekly intervals, than from mercury and iodides. As is the case with a few adults, many of these patients show a persistently positive Wassermann, in spite of long-continued treatment. Just what this means is not yet established. However, every effort should be made to secure a permanently negative Wassermann.

#### IODIDE OF POTASSIUM

Since the advent of salvarsan, iodide of potassium is occupying a less important place in the therapy of syphilis. It is particularly valuable, in stimulating the healing of lesions where there is a considerable cellular infiltration, and in periostitis, in specific headache, and in nerve syphilis. Many men give it as a routine in courses when the patient is resting from more active treatment.

#### QUESTION OF CURE

It is not an easy matter to say when a patient is cured. There are undoubtedly a few patients cured with a comparatively small amount of treatment, but in laying down general rules governing cases, safety can be secured only by giving each enough to cure the majority. This may result in overtreating some cases, but better overtreat any number of patients with so serious a disease as syphilis than undertreat one. In the first place then, a cure can only be considered after the patient has had a sufficient amount of treatment. Emphasis should be placed on this point, as many patients have been told they were well on securing a certain number of negative blood tests, even if only six or eight months' treatment had been given. Negative Wassermann tests secured during the period of treatment are not sufficient evidence upon which to pronounce a cure. They indicate only that satisfactory progress is being made. It is extremely important that all patients who have concluded the necessary treatment be kept under observation and that the question of cure be not settled until the end of this period. It is considered necessary that a period of at least two years be devoted to observa-

tion, during which time tests be made of the blood, and in many cases of the spinal fluid. Examinations should be made at least every three to six months, including a blood Wassermann, and most syphilologists agree that a final spinal fluid test should also be made in all cases. As to what should be done with a patient showing some positive test or symptoms, during the observation period, consultation is suggested. It is possible in so brief a paper to cover only majority cases, and no effort has been made to suggest treatment for exceptional individual cases.

# Abstract of Current Syphilis Literature

It is the purpose of this JOURNAL to review so far as possible all literature on syphilis as it appears in other medical periodicals and to present it in abstract form. Authors are requested to send abstracts or reprints of their papers to the Associate Editor, Dr. Wm. H. Deaderick, Dugan-Stuart Bldg., Hot Springs, Arkansas.

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WM. H. DEADERICK, M.D., EDITOR

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THE TEACHING OF SYPHILIS IN UNDERGRADUATE SCHOOLS.—Walter James Heimann, New York. *Journal of Cutaneous Diseases*, 1917, vol. xxxv, p. 740.

Reflection of the significance of the disease to the individual and to the race is amply convincing that its proper instruction is a matter of first rate sociologic importance. To raise the standard of teaching to a level worthy of the import of the malady, several changes in medical school organization are essential. First, the department concerned with the subject may no longer be counted one of secondary importance. Syphilis, with dermatology, must at last be considered a major medical subject. Secondly, the chair of this department must be directly represented in the faculty. This is essential, so that the head of the department may be in immediate touch with the heads of other closely concerned departments, notably those of internal medicine, pathology, bacteriology, and neurology. The purpose of this is to facilitate the planning of a consistent curriculum in which the various phases of the disease may be emphasized. Changes in the plans of teaching, modifications in the methods of instruction, the incorporation of new ideas determined by progress, must be accomplished through immediate representation. This is an important element in organization. But it is obvious that the man responsible to the community for instruction in the disease at present most important to mankind must be the official and scientific equal of all other members of the faculty.

THE TEACHING OF SYPHILIS.—John A. Fordyce, New York. *Journal of Cutaneous Diseases*, 1917, vol. xxxv, p. 717.

We are primarily concerned in instructing students in the art of diagnosis and treatment. This can best be accomplished first, by

demonstrating a large group of cases in all stages of the disease, and pointing out the characteristic features, second by emphasizing the relative value of clinical observations as compared with laboratory methods, and instructing students in the intimate details of how to employ and correlate both procedures, third by developing and teaching a proper therapy in the various stages of the disease with indications and contraindications for the specific drugs and the by-effects of each. The department of syphilology in a teaching institution is considered as to organization under the following scheme: (1) The Head of the Department and a Trained Staff. (2) The Equipment of the Clinic. (3) The Necessity of a Follow-Up System in Connection with a Syphilis Clinic. An ideal syphilis clinic should be a center of instruction for the undergraduate and postgraduate, where accurate knowledge may be acquired and disseminated. An endeavor is made to give to the student a comprehensive clinical and pathologic picture of the disease by the demonstration of cases, models, photographs, lantern slides, and from the histologic and gross pathologic material, aided by the special laboratory methods which are available. As the teacher of syphilis has at his command a sufficiently large dermatologic clinic, he is in a position to illustrate the differential diagnosis of syphilitic rashes and those which resemble it in the early, as well as in the late, stages of the infection. The relation of nervous system involvement in early syphilis to the subsequent development of tabes, paresis, and other forms of cerebrospinal syphilis, is frequently emphasized so that the student may always have in mind, when treating an early case of syphilis, the possibility of invasion of the spinal fluid. A syphilographer can obtain valuable aid in diagnosis from the neurologist, the ophthalmologist, the laryngologist, or the internist, and all of these departments in a medical school should cooperate.

TEACHING OF SYPHILIS IN SCHOOL AND HOSPITAL.—C. Morton Smith, Boston. *Journal of Cutaneous Diseases*, 1917, vol. xxxv, p. 726.

Syphilis is more than a genitourinary or a dermatologic manifestation, and should be treated and taught in a department of its own. The teaching of syphilis should include an interest in all the activities in the subject that are being carried out in all departments, from the prenatal clinic to the necropsy laboratory. A Wassermann test should be taken on all applicants. A department of syphilology must have beds in the ward, where cases not suited for an ambulatory may be studied and treated. Cases of visceral syphilis should be cared for, so the department must have a skilled internist. Laboratory facilities for studying biopsies and carrying out research work must be provided. A social service worker in the clinic and an effective "follow-up" system are indispensable.

SYPHILIS IN THE AUSTRIAN ARMY.—Hecht. Wiener klinische Wochenschrift, vol. xxix, No. 51.

Hecht states that in his corps records are now kept of every man with venereal disease, and a certain mark opposite the name of a man on the register indicates that in no circumstances is he to be granted home leave. This restriction of home leave had previously been enforced for typhoid carriers. Hecht adds that no one seems to class the venereal diseases with infectious diseases, but he is convinced that this neglect to apply the measures that have been found reliable with other infectious diseases will avenge itself sooner or later. He estimates that the number of syphilitics in the Austrian army now must certainly be several hundreds of thousands, and complains that they are being treated in hospitals, while sound and healthy men are being shot down in their stead. This actually places a premium on sexual infection, for the healthy have no chance of a few months' respite in the hospitals from the fighting. The effect likewise is to spare the syphilitics, while the sound get killed off. He makes the very reasonable suggestion that the diagnosis should be the signal for sending the man to the front. This would have a deterrent effect; at present many prefer to take their chances with syphilis rather than with the enemy's shells. Hecht thinks it might be possible to form special companies of syphilitics as soon as the ulcers have healed over, so that the treatment could be conveniently continued and applied on the firing line, while infection of other troops would be prevented. Neisser long insisted that courses of salvarsan and mercury could be given perfectly well in the trenches. Hecht declares that it is impossible to reiterate too often the frightful danger for the populace from syphilitics in the primary phase. Since the war began, a total equivalent to sixty divisions have been temporarily withdrawn from the fighting for venereal diseases. In conclusion, Hecht insists on the necessity for enlightening the public in regard to the danger of venereal disease in candidates for matrimony.

SYPHILIS AMONG ADMISSIONS TO ELGIN STATE HOSPITAL.—E. W. Fell, Elgin, Ill. Illinois Medical Journal, October, 1917.

Sixteen per cent of admissions to Elgin State Hospital are syphilitic, about 22 per cent of males and 9.5 per cent of females. Paresis forms about 12 per cent of the admission rate, 19 per cent of males and 5.5 per cent of females. At the present time prophylaxis is our only effective means of combating paresis, no known drug or method of treatment being of any value. Every case of paresis should, however, be treated intensively with mercury and neosalvarsan because the coexistence and extent of meningovascular lesions can not be determined absolutely by any clinical or laboratory means.



Excluding the purely syphilitic psychoses, about five per cent of admissions are syphilitic, men somewhat more frequently than women. There is no evidence in these cases that the infection has anything to do with the mental trouble. There is reason to believe that the percentage of syphilis in the general adult population is approximately the same as the percentage of incidental syphilis in the intake of a large state hospital.

**SOME POINTS ON MALIGNANT SYPHILIS.**—Charles F. Marshall, London, England. *Urologic and Cutaneous Review*, 1917, vol. xxi, p. 579.

As regards the constitution of the patient, it is remarkable how many of the victims of this form of the disease are otherwise in robust health. The idea that malignant syphilis only attacks the persons of broken-down constitution must be abandoned. Next as regards the virus. Here there are two possibilities: (1) a specially virulent form, or even a variety, of the spirochete; (2) secondary infection with other organisms. The prognosis of malignant syphilis is on the whole fairly good, although the disease may cause much destruction of tissue before it is cured. In fact, it appears to have a greater natural tendency to cure than other forms of syphilis. It is possible that the virulence of the disease is exhausted in the early stages, and also possible that such cases are less liable than ordinary cases of syphilis to after effects such as parasyphilis. Although the etiology of malignant syphilis is complicated and the subject of divers theories, there is more unanimity in opinion as regards its treatment. The chief characteristic of this form of syphilis is that it responds less to the normal antisymphilitic treatment than other forms of the disease. Not only this, but mercurial treatment is contraindicated during the active period of the disease at any rate, and should be given with caution during the convalescent period. Iodide of potassium is useful, especially in conjunction with decoction of sarsaparilla. But the essential treatment of malignant syphilis is tonic. Quinine and iron are useful, and a nourishing and stimulating diet is important. Sea air and sea bathing are of much benefit. Opium is often indicated. Local treatment is essential. This consists in disinfection of the ulcers by means of prolonged baths containing permanganate of potassium, cyllin or some other nontoxic disinfectant, and the subsequent application of dressings and powders of a similar nature. The treatment of malignant syphilis should be tonic and stimulatory rather than antisymphilitic.

**SYPHILIS OF THE JOINTS.**—James K. Young, Philadelphia. *Medicine and Surgery*, 1917, vol. i, p. 836.

Articular syphilis may manifest itself either in the hereditary or the acquired forms of the disease. In the hereditary syphilis, four

different varieties may be enumerated. First, simple serous synovitis, marked by excessive effusion and with little destruction of cartilage. Second, a chronic synovitis with chronic hyperplastic degeneration of the synovial membrane. Third, it may exhibit itself as an osteochondritis of a degenerative type of inflammation, accompanied by chronic synovitis and necrosis of the epiphyses. Fourth, a chronic arthritis, secondary to an osteomyelitis, a periostitis, or an osteitis of the shaft of the long bones. The treatment of the different forms of syphilitic arthritis will vary according to the type of the disease. If the Wassermann reaction is positive, suitable doses of arsenobenzol, or neosalvarsan should be employed until the test becomes negative, after which mixed treatment should be administered for a period of six months. Another Wassermann test should then be made, and if positive, treatment should be repeated; if not, the mixed treatment should be continued in diminishing doses for a year. The effect of these mercurial preparations upon hereditary joint lesions is most beneficial and prompt. In the most common form, osteochondritis, after removing the necrotic tissue freely from the joint by surgical means, with knife, curette, etc., pain disappears and healing begins almost immediately after the administration of mercurial preparations. The joint should be then supported by a plaster of Paris cast and contractions carefully guarded against in the chronic forms by suitable orthopedic apparatus; in the later stages, massage, baking, and counterirritation by means of iodine. Oleaginous preparations will be found of considerable value in this class of cases. In the mixed type of infection, where syphilis and tuberculosis are both present, the former may be treated with arsenical preparations, just mentioned, and also by means of the mixed treatment, and the tuberculous condition will require x-ray applications every two or four weeks, the administration of tonics, good hygienic surroundings, and possibly change of climate. In Charcot's lesion of joints, resort should be made to spinal puncture both for diagnostic and therapeutic purposes. Because of the occasional occurrence of paralysis following spinal puncture, the preparation to be injected should always be mixed with the withdrawn spinal fluid, taken from the individual under treatment.

SYPHILIS OF THE BLADDER.—H. A. Fowler, Washington, D. C. *Journal of the American Medical Association*, 1917, vol. lxix, p. 1399.

In the case reported there are several points of interest. The symptoms were those of a severe cystitis coming on without apparent cause. The urine showed an acid total pyuria together with red cells and bacteria. The condition suggested tuberculosis of the urinary tract with a secondary infection, probably colon bacillus. Repeated search for tubercle bacilli, however, was negative. There

were no changes to be made out in the epididymis, vesicles, or prostate. The general glandular enlargement aroused suspicions of syphilis, and these were strengthened by a strongly positive Wassermann test. Cystoscopy revealed, in addition to a solitary ulcer about the right ureteral opening, a peculiar appearance of the mucous membrane; but nothing about the cystoscopic findings could be considered characteristic of syphilis. Certainly the ulcer might easily have been mistaken for tuberculosis. The marked and prompt improvement in the symptoms and the ultimate disappearance of the vesical lesion following salvarsan alone seemed to justify the diagnosis of syphilis. It is of interest to note that no history of syphilis was obtained in this patient.

**PULMONARY SYPHILIS.**—Thomas F. Reilly, New York. *The Medical Adviser*, 1917, vol. vi, p. 410.

Clinically one may make two distinct classifications of pulmonary syphilis: (1) tracheobronchitis; (2) syphilis of the deeper portions of the lungs. To this may be added a third, as evidenced by the influence of syphilis on other diseases of the lungs. The lesions are: (1) a diffuse circular exudation surrounding the tracheal or bronchial tube; (2) gumma producing a tumor formation in the lumen of the bronchi or trachea. The symptoms are: (1) paroxysmal, brassy cough like that of aneurysm; (2) dyspnea; (3) change in voice; (4) difficulty in coughing; (5) acute suffocative attacks; (6) stridor; (7) drawing in of the supra- and infraclavicular spaces. On physical examination there is enfeeblement of respiratory murmur below the obstruction. When syphilis affects the deeper portions of the lungs, it does so either as: (1) a widespread infiltration leading to fibroid changes; (2) as an endarteritis; (3) as gumma. As to signs and symptoms: (1) there is dullness on percussion; (2) dyspnea and cough with slight febrile elevation and a relatively slow pulse; (3) occasionally there are night sweats, profuse expectoration, and blood.

**PULMONARY SYPHILIS.**—M. Ford Morris, Jr. Chelsea, Mass., *Medicine and Surgery*, 1917, vol. i, p. 949.

Inherited syphilis of the lungs is of two kinds: circumscribed and diffuse, the former being known as "gumma" and the latter as "pneumonia." Hereditary pulmonary gummata are rare and differ in no way from the acquired form. The diffuse form is known either as "white pneumonia" or "interstitial pneumonia," but these two lesions usually are combined. Interstitial pneumonia often is associated with pronounced prenatal luetic lesions elsewhere. The life of a child with this condition is not prolonged. The most characteristic features of interstitial pneumonia are a small-celled infiltration of the interalveolar connective tissue and a marked

increase of the interlobular connective tissue. In acquired syphilis, the chief pulmonary lesions are (1) gummata, (2) bronchopneumonia, (3) fibroid induration, or chronic interstitial pneumonia, and (4) a progressive destructive disease, the so-called "syphilitic phthisis." Gummata in the lungs are similar to gummata elsewhere. They range in size from that of a small pea to that of a hen's egg, and occur in all parts of the lung, but most frequently within the substance of the lung near the hilus. Gummata of the lung may caseate, but usually tend toward the formation of cicatricial tissue, which causes a shrinkage of the surrounding lung substance, as well as a dimpling of the lung surface and the adherent pleura. There is much doubt concerning the existence of a syphilitic bronchopneumonia. Fibroid induration consists, either separately or combined, of long strands of connective tissue which divide the lobes and groups of lobules, which often radiate from the hilus of the lung and which more or less surround the bronchi and vessels; of patches of sclerosis, and of diffuse fibrous changes affecting a lobe or even an entire lung. The coexistence of pulmonary syphilis and tuberculosis is not so infrequent as some suppose. The presence of tuberculous processes in the lung simultaneously with the less consuming lues may account, in a measure, for the infrequency of the syphilitic diagnosis.

The prognosis in uncomplicated pulmonary syphilis should, of course, be guarded. But under intelligent treatment, begun before the patient has lost the power of resistance, the condition usually progresses favorably. When pulmonary syphilis and tuberculosis coexist, as must be the case so often, the chances for recovery are lessened. Coughing is probably the earliest and most frequent symptom, which results from irritation of the respiratory tubes or from changes within the lung. The coughing usually produces much offensive sputum which does not contain tubercle bacilli. Hemoptysis is also a very common occurrence in pulmonary syphilis. Sometimes the blood is just sufficient in amount to tinge the sputum, but at other times it is more profuse. Pain, emaciation, and night sweats may be present. Dyspnea occurs not infrequently. In cases in which the disease is extensive in its location and fulminating in its character, fever may be quite high, which pyrexia is usually of the tuberculous type. The physical signs are, of course, dependent upon the character of the lung lesion. Consolidation and cavity formation are recognized by their characteristic signs. The treatment of pulmonary syphilis is not different from the treatment of the disease in other organs.

**ACUTE SYPHILITIC GLOMERULONEPHRITIS.**—Douglas Symmers, New York City. *Interstate Medical Journal*, 1917, vol. xxiv, p. 1010.

In early secondary syphilis the appearance of moderate quantities of albumin and casts in the urine is not frequent. It represents

a response to irritation, and is attended, histologically, by degenerative changes in the epithelium of the convoluted tubules and by the presence of small quantities of coagulated serous exudate in the glomeruli. It is a transient process and complete recovery occurs when the irritant is withdrawn. Formerly, the urinary changes in question were ascribed to the influence of treatment by mercury, but this view has since been abandoned. On the other hand, syphilis is sometimes the cause of acute inflammatory changes in the kidney of such nature and extent as permanently to disable the kidney or even to cause death. The condition is casually mentioned in textbooks in clinical medicine and pathology, but, in bedside work and in the experience of the autopsy room, acute syphilitic nephritis is exceedingly rare. In a case recently investigated postmortem at Bellevue Hospital, death occurred after a brief illness and the changes in the kidney were of the same type as those encountered in the acute nephritis of scarlet fever.

**PRIMARY SYPHILIS OF THE GUMS.**—Achille Breda, Giorn, ital. delle Mal. ven. e delle Pelle, Jan., 1916.

Breda records three cases where primary sores occurred on the gums. As that situation is rarer on the lips and tongue, he gives a full report of the differential diagnosis. The sore was situated on the anterior aspect of the gums, painless, of rapid growth, and accompanied by the usual glandular enlargement and subsequent rash. The object in reporting the cases is to draw attention to the differential diagnosis. It has to be distinguished from a swelling due to periostitis of the bone from injury, coma, and fibroma. The accompanying enlargement of glands also leads to confusion with new growths. The syphilitic lesion can be diagnosed by its history of short duration, and the fact that it is localized to the mucous membrane. It occurs more on the anterior than the posterior surface of the gum opposite the front teeth. It is not usually large, is sharply defined, and of semilunar outline. Elevated, pedunculated, lobulated or massive swellings are not likely to be syphilitic.

**SYPHILIS OF THE THYROID.**—J. A. Storck, New Orleans. New Orleans Medical and Surgical Journal, 1917, vol. lxx, 417.

The thyroid is not infrequently involved in both early and late syphilis. In the author's experience, thyroiditis is the most common condition met with in syphilis, but, from the observation of others, gumma and other conditions occur. While the thyroid is at times involved in the adult syphilitic, it is sometimes found in the young, but most often of all in infants. The thyroiditis occurring in syphilis is favorably influenced by intensive antisiphilitic treatment.

A STATISTICAL STUDY OF THE CAUSES OF ABORTION.—G. D. Royston, St. Louis. *American Journal of Obstetrics and Diseases of Women and Children*, 1917, vol. lxxvi, p. 582.

More than 20 per cent, probably over 25 per cent of all abortions are induced. Sixty per cent of all induced abortions result in more or less permanent sterility. Abortions induced by the midwife, the patient herself, and by the physician, rank in danger in the order named. Neither married state, church affiliations, nor the fear of ill health will deter a woman once determined to interrupt her pregnancy. A positive Wassermann reaction is obtainable in about 25 per cent of all women who have aborted. Less than one-third of the syphilitic women give any history or show any physical signs indicative of the disease. Only by a routine Wassermann reaction can syphilis in the obstetric-gynecologic patient be detected. Syphilis interrupts pregnancy at any and all periods of gestation. Syphilitic women abort in more than 60 per cent of their pregnancies. A renal deficiency interrupts pregnancy only in the event of a renal decompensation which produces symptoms, as a rise in blood pressure, lassitude, headaches, insomnia, or somnolence, vague discomfort, irritable uterus and a drop in the phthalein output. These indications are that an interruption of pregnancy is impending and are often amenable to treatment. Pregnancy may be interrupted as a result of renal deficiency at any period of gestation. The phthalein test is of great value, though not an infallible index to the true renal condition. Extragenital factors can produce abortion and must be investigated if subsequent pregnancies are to result in living children. Sixty-five to 90 per cent of all women who have aborted will show some pathologic lesion in the genitalia. A poor state of nutrition influencing an interruption of pregnancy is usually but a symptom of a more important underlying condition, as syphilis, impairment of the heart, lungs or kidneys.

A FURTHER REPORT OF EIGHT CASES OF SYPHILIS OF THE STOMACH.—William A. Downes, New-York City. *Surgery, Gynecology and Obstetrics*, 1917, vol. xxv, p. 361.

Syphilis of the stomach may be congenital or acquired. Two of the cases here reported were undoubtedly of congenital origin; one in a female, aged 14, the other in a male, aged 17. A history of stomach trouble extending back many years was obtained in both instances. In the 6 cases of the acquired type, two gave definite histories of chancre, while in the remaining four, there was no history of primary infection. In this group there were 3 males and 3 females, the youngest was aged 22, the oldest 63. The lesions vary from a diffuse syphilitic gastritis with a round-cell infiltration spreading through the submucous tissue, to localized or general gummatous infiltration

involving all the coats. These gummatous deposits may be single or multiple and not infrequently ulcerate. One portion of the stomach wall may remain infiltrated while another passes on to ulceration or in the healing stage becomes cicatricial. The irritation of the peritoneal coat results in perigastric adhesions of varying extent. Definite pyloric obstruction may occur as a result of the gummatous infiltration, cicatrization of the ulcer, or from the perigastric adhesions. It is for the relief of this complication that surgery plays an important role in the treatment of the disease. Besides the lesions in the stomach wall, other evidence of lues are usually found, such as changes in the liver capsule, gummata of the liver, extensive involvement of the gastrohepatic and gastrocolic lymph glands as well as other evidence of a generalized syphilis.

The symptoms of gastric syphilis, taken as a whole, vary but little from those of other stomach lesions of similar extent; however, upon careful analysis, several striking differences become apparent. The pain which is a most constant symptom lacks the periodicity of that occurring in the average simple ulcer, and it is much more influenced by the taking of food. It is frequently worse at night and is often referred to as gnawing the character. Vomiting is a persistent and annoying symptom. It was present in all the author's cases. Hemorrhage is not so frequent as in peptic or duodenal ulcer, which is rather remarkable when the duration and extent of the lesion are taken into consideration. A striking feature of the disease clinically is the rapid, and not infrequently, extreme loss of weight. Gastric analysis was made in 6 of the cases with the following results. In cases 1, 7 and 8, free hydrochloric acid absent, combined acidity 32, 16, and 14, respectively; in these cases the lesion was extensive, involving a large portion of the stomach wall. In cases 2 and 3, in which the lesion was confined to the pylorus, free hydrochloric acid was 30 and 36, with a total acidity of 52 and 70. In case 4, in which there was hourglass constriction, the analysis showed free hydrochloric acid 13, total acidity 34. Lactic acid was absent in each case. The guaiac test for blood was positive in 5 cases. These findings would seem to suggest that there is an absence of free hydrochloric acid and a low total acidity in the cases with extensive involvement of the gastric mucosa. The diagnosis of this condition can be established with a fair degree of certainty if the clinical and laboratory findings are given proper consideration. In the congenital cases, the family and previous history of the patient, his general development and appearance, with the symptoms of chronic stomach trouble should arouse suspicion. The acquired cases may be more difficult to diagnose, but the past history plus unusual symptoms should suggest that the case is out of the ordinary. In both types the course of the disease differs from the simple gastric or duodenal ulcer, in that it is influenced but little by dieting and the ordinary methods of treatment, and it is unlike malignancy in that there is not the

steady and continuous progress to a fatal termination. A positive Wassermann reaction with roentgenographic findings of persistent and unusual deformity of the stomach establish the diagnosis beyond much doubt. In view of the accuracy of modern laboratory aids to diagnosis, one hesitates to refer to the so-called therapeutic test, but the value of antisyphilitic treatment in confirming the diagnosis of syphilis in general can not be ignored. Such treatment may be of temporary benefit in ordinary ulcer or even cancer of the stomach, but the improvement is of short duration; whereas, in the luetic cases, there is almost immediate and continued relief from symptoms.

PSYCHOSES OTHER THAN PARETIC DEMENTIA IN SYPHILITIC INDIVIDUALS.

—Alfred Gordon, Philadelphia. *Journal of the American Medical Association*, 1917, vol. lxix, p. 1409.

An analysis of the cases described in this study tends to show that while the mental disturbances during the secondary stage of syphilitic infection could be considered with a great degree of certainty as directly dependable on syphilitic toxins, the same degree of certainty can not be entertained with regard to a direct relationship of psychosis developed during the tertiary period of syphilis. In the former, the mental manifestations are in all analogous to those which we observe in toxi-infectious states from any origin. The confusional and delirious conditions, as well as the hallucinations, ran parallel with secondary manifestations and with fever. When the latter disappeared, the former commenced to improve. Besides, the antisyphilitic treatment had a very manifest and favorable effect on the mental phenomena. In the other series of cases we find various psychoses which develop many years after the initial infection and which in all respects present the typical pictures of classical psychosis, such as Korsakoff's syndrome, manic-depressive insanity, melancholia and dementia paranoides. Great difficulty is encountered and no definite opinion can be formed with regard to a direct relationship between the psychoses and the infection which occurred many years previously. On the other hand, it has been observed that those psychoses in syphilitic individuals presented some modifications which could justly be attributed to the influence of syphilitic toxins. In the light of our present knowledge we are not warranted as yet to claim for syphilis the ability to create *per se* the well-established forms of insanity which we observe without a syphilitic infection. The literature on the subject is very meager, and a considerably larger number of carefully collected records will be necessary to enable us to establish in a more definite way a causal relationship of syphilis to psychoses. For the present, no final claim can be made as to a type of mental disease characteristic of syphilis. On the other hand, from the observations which we possess we are not authorized to reject entirely the possibility of psychoses being the result of syphilis.



HEREDITARY SYPHILIS OF THE INTERNAL EAR.—Oscar Beck, *Medizinische Klinik*, 1916, No. 12.

Beck distinguished the following main types: 1. Isolated involvement of the acoustic apparatus. 2. Simultaneous involvement of the cochlear and vestibular apparatus. 3. Involvement of the static labyrinth alone. He takes up only the first type of the disease, the frequency of which amounts to 20 to 30 per cent in hereditary syphilitic children. Three forms are described according to symptomatology: 1. The apoplectiform, in which the onset of the deafness is very sudden, sometimes overnight, the static function remaining undisturbed. The usual age of recurrence is the tenth year. Prognosis is absolutely unfavorable. 2. Insidious form, the age of occurrence being about the same as in the apoplectiform, often associated with Hutchinson's triad. 3. In this form subjective noises are most prominent, the hearing capacity apparently remaining unimpaired. The author also points out various analogies between the clinical symptoms and anatomic findings in otosclerosis and hereditary syphilis, but of course, there are essential differences. The pathologico-anatomic processes in hereditary syphilitic disease of the internal ear are (1) degenerative inflammation of the acoustic nerve; (2) secondary inflammatory processes of the acoustic nerve; (3) periostitic process in the labyrinth capsule with endolabyrinthine changes.

WASSERMANN COMPLEMENT-FIXATION TEST FOR SYPHILIS.—J. Wheeler Smith, Jr., New York City. *New York Medical Journal*, 1917, vol. cvi, p. 1031.

There can be no question that the addition of cholesterol to the alcoholic extract renders the latter more powerful as an antigen and that considerably more positive results are thus obtained in the practical testing of human serums. Smith and MacNeal have recently reported comparative studies of different antigens and of different temperatures of incubation in the Wassermann test. In one study Wassermann tests were performed by three methods upon 496 identical specimens from 477 patients. In the first method a cholesterol reinforced antigen was employed and the first incubation was carried out at 37° C. In the second method a simple alcoholic extract was used as antigen, with incubation also at 37° C. In the third method this latter antigen was again employed, but the first incubation was carried out in the refrigerator for a period of four to twenty-four hours. The last method proved more sensitive in the group of known syphilitics than the other procedures tested. Furthermore, a positive result thus obtained proved to be more trustworthy evidence of syphilis than did positive results obtained with the cholesterolized antigen and first incubation at 37° C. In

the second study, tests were performed by six different methods upon 501 identical specimens from 457 patients. Three antigens were employed, cholesterolized alcoholic extract of beef heart, simple alcoholic extract of beef heart, and the acetone insoluble lipid fraction of alcoholic extract of beef heart, prepared according to the method of Noguchi. Each of these antigens was used at two different incubation temperatures for fixation of the complement, 37° C. and 80° C., the subsequent incubation after addition of sensitized erythrocytes being carried out at the higher temperature. Upon known syphilitics, the cholesterolized antigen at 8° C. gave the largest number of positive reactions, being followed, in order of efficiency, by the plain antigen at 8° C., cholesterolized antigen at 37° C., acetone insoluble antigen at 8° C., the same at 37° C., and last the plain antigen at 37° C. Reactions considered to be false positives were obtained eight times with the cholesterolized antigen at 37° C., and five times with the cholesterolized antigen at 8° C., but the simple alcoholic extract of beef heart gave no false positive reactions of any degree of fixation in this series of 501 tests. It would seem from these studies that a simple alcoholic antigen with the first incubation carried out in the ice box for four to twenty-four hours, is sufficiently sensitive in the detection of syphilis. Furthermore, a positive result thus obtained is much more trustworthy evidence of syphilis than is a positive fixation with a cholesterolized antigen not only when used at 37° C., but also when the incubation is in the ice box.

THE COLLOIDAL GOLD TEST.—J. H. Black, Louis Rosenberg, and R. B. McBride, Dallas, Texas. *Journal of the American Medical Association*, 1917, vol. lxix, p. 1858.

Singly distilled water may be stored satisfactorily in clean glass for many days. Protected solutions are usually due to unclean glass. Reagents may be used satisfactorily as stock solutions. If technic is carefully followed, turbid solutions are due to slow or irregular heating and can not be corrected. Formaldehyde should be added at from 90° C. to boiling. Solutions poor because of use of minimal amounts of alkali or formaldehyde may be corrected, the latter so that they may be used clinically. The use of oxalic acid is not necessary and is possibly occasionally responsible for failure of reduction. The presence of carbon dioxide is of no consequence. Solutions alkaline at the time of preparation or on standing may be made neutral by reheating and adding formaldehyde. Solutions showing a slight shimmer may be used satisfactorily. Solutions definitely alkaline at the time of preparation, if of good color, may be satisfactorily used. Those alkaline from standing give irregular curves. A colloidal gold reaction typical for syphilis is nearly constant in cases of syphilis of the central nervous system. This reaction is

more delicate than the Wassermann tests on the blood and spinal fluid and more reliable than pleocytosis and globulin content. Curves are, of course, given with other conditons than syphilis, but the curves given are believed to be specific. The test is the most reliable of the various tests as a diagnostic aid, and is the best guide for prognosis during treatment, probably tending to become negative in a regular and constant order. Known paretics always give a paretic curve; however, there is obtained occasionally a paretic curve in other phases of central nervous system syphilis. There is no provocative colloidal gold test. The presence of red blood cells or plasma in the spinal fluid often vitiates the result of the test.

**THE WASSERMANN REACTION IN DUPLICATE.**—Maximilian Schulman, New York City. *New York Medical Journal*, 1917, vol. cvi, p. 931.

The author concludes that reliable laboratories, working with a closely similar technic, will report concordant results, and that a clinician who exercises judgment in the application of the technicians' reports will always be aided and never misled.

**THE SIGNIFICANCE OF CERTAIN DENTAL STIGMATA OF CONGENITAL SYPHILIS.**—Joseph S. Wall, Washington, D. C. *Archives of Pediatrics*, 1917, vol. xxxiv, p. 768.

The dental stigmata pathognomonic of hereditary syphilis are the following: (1) Hutchinson's teeth, (2) cuspal erosions of the first permanent molar; (3) multiple and systematic dystrophies of the permanent teeth. These systematic, and at the same time symmetrical, alterations are dependent upon a general pathologic process of considerable duration, which produces an arrest of development of the dental follicles during intrauterine life (sixth month and upwards) resulting in the changes in the first molars; or, during extrauterine life (just after birth) producing Hutchinson's teeth and the atrophy of the canines. Any clinical clue to the existence of congenital syphilis before the onset of a destructive keratitis, which not rarely is one of the latest manifestations, must be recognized as a sign of considerable importance, and more especially so when it points the way to effective therapeusis.

**THE WASSERMANN REACTION AND PULMONARY TUBERCULOSIS.**—James S. Ford, Loomis, New York. *New York Medical Journal*, 1917, vol. cvi, p. 679.

The author believes that only a persistently positive Wassermann reaction should make one certain of a diagnosis of syphilis in a patient suffering from pulmonary tuberculosis. A cholesterinized antigen, in this series, has made practically little difference in the ultimate results.

ON THE USE OF THE EMANUEL-CUTTING MASTICHE TEST IN EXAMINING SPINAL FLUID FROM PSYCHOPATHIC SUBJECTS.—Curtis E. Smith, Boston. *Boston Medical and Surgical Journal*, 1917, vol. clxxvii, p. 557.

A normal fluid causes no change in the mastiche test solution in any tube. The control tube does not precipitate, as was the case using the original method. Between the unchanged and the maximum change; i. e., complete precipitation with clear supernatant fluid, we may recognize certain gradations. Thus in many cases there is produced a very marked clouding, through which light is not transmitted. In another type, light is very faintly transmitted. Again, there may be a perceptible clouding with fairly good transmission of light. Finally, there may be a change so faint that it is recognizable only in comparison with the control. These changes can be noted by the number system, as in reading the gold reaction. We then have a series, ranging from 5 to 0, and can compare mastiche and gold curves, if such exist. Because of these facts, it seems that the mastiche test, as modified by Cutting, has a distinct place in the clinical laboratory. Because of the ease and accuracy of examination, it may well be used to determine in which cases the more complicated gold test should be done.

THE DIAGNOSTIC VALUE OF SPINAL FLUID AND WASSERMANN TESTS IN PSYCHIATRY.—E. W. Fell, Elgin, Ill. *American Journal of Insanity*, July, 1917, vol. lxxiv.

At Elgin State Hospital, in the past year and a half, 500 admissions (not consecutive) in whom paresis was for one reason or another suspected, have been given serum and fluid Wassermann tests, globulin tests, and cell counts. Of these 215 were luetic psychoses and 285 nonluetie psychoses. The gold chloride test was not used. The number of cases of taboparesis and cerebrospinal syphilis was not sufficient to draw any conclusions except to say that the findings were less constant than in paresis. (1) Establishing the existence of paresis. In paresis the tests failed as follows: Globulin increase 2 per cent, pleocytosis 10.5 per cent, serum Wassermann 7 per cent, fluid Wassermann 4 per cent. In the non-luetic psychoses the tests were positive as follows: Globulin increase 5.5 per cent, pleocytosis 3.5 per cent, serum Wassermann 9.5 per cent, fluid Wassermann none. Cell and globulin increase in nonluetie psychoses was found especially in organic cases where a differentiation was important. There is abundant evidence that positive fluid findings may occur without paresis in the primary and secondary stages, and it is probable that they occur without the mental symptoms of paresis in the "pre-psychotic" stage. It is not argued that a positive spinal fluid Wassermann is of itself conclusive

evidence of paresis, nor that a negative test excludes paresis, but it is so constantly positive in the one and negative in the other that it is of the greatest value, in a case where a differentiation must be made, in distinguishing between a luetic and nonluetic psychosis. (2) The extent of the parietic process can not be determined with any degree of accuracy by laboratory tests; it can only be said in a general way that globulin and cell increase seem more marked in the more rapid cases. (3) The distinction between a parietic process and a tertiary luetic process, or the extent to which each is present, can not be determined in the laboratory. The gold chloride test is of some help in this direction, but the therapeutic test is the only one of much value. (4) The diagnosis of the combination of paresis with a functional psychosis should be made with extreme caution. (5) In making a diagnosis of recovery in a case of paresis which has cleared mentally, the following conditions should be considered: 1. A functional psychosis in the primary or secondary stages of syphilis. 2. A functional psychosis in the "pre-psychotic" stage of paresis. 3. A remission in paresis. It should be remembered that the first two occur quite infrequently, the last very frequently, the spinal fluid findings remaining positive.

**THE WASSERMANN REACTION WITH LARGE AMOUNTS OF PATIENT'S SERUM.**—Anna I. van Saun, Albany, N. Y. *Journal of Laboratory and Clinical Medicine*, 1917, vol. iii, p. 62.

The use of a large amount of serum does not, in the author's experience, change a serum giving a negative reaction to one giving a positive if a double serum control (0.8 c.c.) is used and the result of the test read only when this control is completely hemolyzed. In a number of tests the author has found that the 0.4 c.c. serum control has been extremely slow to hemolyze, and has occasionally fixed complement completely. This result appears to point to a lack of specificity in a test depending on this amount for diagnosis. Since large amounts of serum may of themselves bind complement without the addition of a Wassermann antigen, and since, in the above tests, in almost every instance, controls of double these large amounts of serum did not hemolyze completely, the author does not consider the Kromayer modification a safe method to use for the practical examination of large numbers of sera.

**A STUDY OF TWO HUNDRED AND NINETY POSTMORTEM WASSERMANN REACTIONS.**—Stuart Graves, Louisville. *Mississippi Valley Medical Journal*, 1917, vol. xxiv, p. 111.

Postmortem Wassermann reactions confirmed antemortem reactions in 95 per cent of 38 control cases. Positives were confirmed in serum six hours postmortem, and negative in serum in twenty-four hours

postmortem. In 90.4 per cent of cases showing postmortem anatomic lesions of syphilis, or presenting positive evidence of syphilis in their histories, the sera postmortem gave positive Wassermann reactions. The fact that positive postmortem reactions appeared in thirty-eight cases, which did not present postmortem lesions or historic evidence of syphilis and in which death was due to acute infections, tuberculosis or malignant tumors, cannot be interpreted to mean that the reaction was caused by those diseases, because, in the first place, the histories and autopsies in those cases were not nearly enough complete to rule out syphilis, and in the second place, because sera from 94 patients who died of acute infections, tuberculosis of malignant tumors, examined under similar conditions, gave negative reactions. Only 7 per cent of 282 cases showed negative reactions in the presence of anatomical lesions (aneurysms) characteristic of syphilis. The reactions conformed to the anatomic and historic evidence in 84 per cent of the cases. The fact that only 8, or 3 per cent, of the sera were anti-complementary indicates that the sera were in good condition. The average percentage of specific reactions was almost as high postmortem as would be expected antemortem. The positive reaction appeared in twice as many males as females, in three times as many negroes as whites, and in white females in only 4.3 per cent of the cases examined. The Wassermann reactions, performed on postmortem blood according to the methods followed in the investigation, is a reliable aid to the diagnosis of syphilis.

THE COMPARATIVE VALUE OF THE WASSERMANN, THE COLLOIDAL GOLD AND OTHER SPINAL FLUID TESTS: A STUDY OF 203 CASES.—E. M. Hammes, St. Paul, Minn. *American Journal of the Medical Sciences*, 1917, vol. cliv, p. 637.

The most constant finding in a pathologic spinal fluid is a positive globulin. It is indicative of an inflammatory process, but is of no specific import. Pathologic cerebrospinal fluids usually show some lymphocytosis. However, the number may be normal. Fluids from cases of meningitis almost invariably give a high cell count. As an index of pathologic change in the cerebrospinal fluid the colloidal gold reaction is more delicate than a number of other tests. Normal spinal fluid usually causes no reduction of the colloidal gold. A slight reduction in any of the dilutions is of no diagnostic import, and may occur in normal spinal fluids. Cases of tabes and cerebrospinal lues give a typical colloidal gold curve in the luetic zone. Although in tabes the intensity of the curve is usually greater, it is not sufficiently constant to be of diagnostic value between the two conditions. In paresis the colloidal gold test is sufficiently frequent and characteristic to warrant the term "paretic curve," and is of great diagnostic value. However, it has been observed in cases of

tabes, cerebrospinal lues, multiple sclerosis, brain abscess, and once in puerperal eclampsia. In meningitis the colloidal gold curve usually occurs in the higher dilutions, and is probably of value in the diagnosis of doubtful cases. In spinal fluids with normal findings, except a paretic colloidal gold curve in doubtful cases, the possibility of a multiple sclerosis must be strongly considered. The colloidal gold test is more delicate than the Wassermann test. Spinal fluids fromluetics have given a colloidal gold luetic curve with a negative Wassermann. However, we have never observed a normal colloidal gold curve with a positive Wassermann in the spinal fluid. Exceptions to this are the congenital luetics. Under antiluetic treatment there is usually a reduction in the cell count and globulin of the spinal fluid; frequently the Wassermann becomes negative; rarely is there a change in the colloidal gold test. No spinal test (except the presence of bacteria) is specific. Every test is simply that much cooperative evidence and should be combined with the history of the case and the clinical findings.

OBSERVATIONS ON THE SIGNIFICANCE OF ANTISHEEP AMBOCEPTOR IN HUMAN SERUM, WITH REFERENCE TO COMPLEMENT-FIXATION TESTS FOR SYPHILIS.—M. H. Neill, United States Public Health Service. Hygienic Laboratory Bulletin, 1917, vol. cx, p. 51.

While it can not be denied that natural antisheep amboceptor does reduce fixation when present in positive syphilitic sera, it would appear from certain experiments that the amount of antisheep amboceptor must be quite considerable and the amount of syphilitic amboceptor very small in order to produce a significant effect. It is, therefore, concluded that the presence of antisheep amboceptor in sera is not a valid objection to the use of a sheep cell hemolytic system in performing routine complement-fixation tests, provided the sera to be tested be used in amounts corresponding to not less than 0.1 c.c. for a test with a total volume of 4 c.c. or 5 c.c.

OBSERVATIONS AND TECHNIQUE OF LUMBAR PUNCTURE IN SEVEN HUNDRED CASES.—Y. C. Lott, New York City. Medical Record, 1917, vol. xcii, p. 719.

As an aid in diagnosis of the degree of intracranial pressure or, in the diagnosis of intracranial injury either extradural by pressure or intradural by pressure and bloody cerebrospinal fluid, no more than 5 c.c. should be removed for diagnostic purposes, which is amply sufficient. As a therapeutic measure in drainage of cerebrospinal fluid to relieve pressure in selected acute cases and in infective conditions, the cerebrospinal fluid should always be removed very slowly while the patient is lying down, especially in cases of high intracranial pressure either above or below the tento-

rium. Lumbar puncture is a safe procedure when properly performed. It is therapeutically contraindicated in high intracranial pressure of long standing or patients in profound shock.

THE WASSERMANN AND LUETIN REACTIONS IN TUBERCULOSIS.—H. J. Corper, W. A. Gekler, and H. C. Sweany, Chicago. *American Review of Tuberculosis*, 1917, vol. i, p. 546.

The luetin reaction can not be used as a test for lues in a tuberculosis sanitarium to displace the Wassermann test. The luetin reaction in tuberculous patients with a negative Wassermann gives a high percentage of positive results (47 per cent). On account of this high percentage of reactions not due to tertiary or latent syphilis in tuberculosis patients, the luetin reaction as carried out today with the luetin obtainable on the market is unreliable.

WASSERMANN REACTION WITH GLYCEROLATED HUMAN SERUM MORE THAN A YEAR OLD.—E. H. Ruediger, Manila, P. I. *Journal of Infectious Diseases*, 1917, vol. xxi, p. 508.

Pure glycerol is an ideal preservative for human serum intended for the Wassermann reaction. In order to prevent the serum from becoming anticomplementary, it must be heated to about 56° C. for thirty minutes and then be mixed with an equal volume of glycerol. Serum kept for more than a year gave practically the same results as when fresh and without preservative.

BRUCK'S SEROCHEMICAL TEST FOR SYPHILIS: A REPORT OF 400 CASES COMPARED WITH THE WASSERMANN REACTION.—Curtis E. Smith, and H. C. Solomon, Boston. *Boston Medical and Surgical Journal*, 1917, vol. clxxvii, p. 324.

We present results of the Bruck serochemical test in 405 cases. In 101 of these cases there were definite clinical manifestations of syphilis, in which the Wassermann and Bruck tests agreed positively in 75, or 75 per cent. The two tests agreed negatively in 12 instances, and were at variance in 15. In the group which showed syphilis of the nervous system, we had 64 cases of clinically certain general paresis, in which the Wassermann and Bruck tests agreed in 54 instances, or practically 85 per cent. In other forms of central nervous system involvement the agreement was 100 per cent in the 15 cases tested. In the cases with no apparent involvement of the nervous system the agreement was somewhat less, being 76 per cent. This may be in keeping with the fact that the Wassermann test was not so strongly positive in these cases. The advantages of the test are: (1) The short time required to do the test, (2) the limited amount of apparatus necessary, and (3) the simplicity of the technic.



The disadvantages of the test seem, for the most part, to be bound up in the personal variations that are apt to occur. We are here dealing, most probably, with a quantitative chemical difference in the protein content of syphilitic and nonsyphilitic sera, the nature of which is not understood by us. It is the author's hope that this may be brought to light in the near future in the field of chemistry.

**THE "GEL" TEST.**—Albert Strickler, Philadelphia. *Journal of Cutaneous Diseases*, 1917, vol. xxxv, p. 430.

It is the author's belief that the Wassermann reaction is the best test for lues in our possession today. The Gel test is a step in the right direction, but can not be compared in accuracy with the Wassermann. The acetic acid thorium sulphate test is a more reliable test than the ammonium sulphate test. It is the author's observation that a serum obtained from a healthy, normal individual several hours after a meal, when the products of digestion are thrown into the circulation, may give a positive Gel. It is his hope that possibly a refinement of this test or the development of another test may give us a method of detecting inactive lues.

**A MORE DELICATE WASSERMANN REACTION DEPENDING ON THE USE OF INCREASED QUANTITIES OF BLOOD SERUM.**—P. T. Bohan and L. A. Lynch, Kansas City, Mo. *Journal of the American Medical Association*, 1917, vol. lxix, p. 1222.

At least 10 c.c. of blood should be obtained and as much spinal fluid as can be taken with safety, from 10 to 15 c.c., if possible. After the blood is centrifuged and the clear serum inactivated, it is transferred to a small centrifuge tube to which is added 0.1 c.c. of pure undiluted thoroughly washed sheep corpuscles, shaken and allowed to stand for one-half hour in the ice chest. The serum is again centrifuged, throwing down the sheep corpuscles, and the clear serum pipetted off ready for the test. In this way natural antishoop hemolysin is removed by absorption. A titration for the proper unit of complement is made with a 2.5 per cent suspension of sheep corpuscles, a known titer of immune rabbit serum and a 1:10 dilution of fresh guinea pig serum. This is done in the presence of the different amounts of serum or spinal fluid to be used in the test: in the case of blood serum, 0.1, 0.3, 0.5 and 1 c.c. The serum is taken from a known negative case. When working with spinal fluid, the titration is done for amounts as high as 10 c.c. The spinal fluid being hypotonic for sheep cells, it becomes necessary to add sufficient sodium chloride to make an isotonic solution. The proper units of complement having been determined, the tests are set up, each serum being run in the amounts mentioned, namely, 0.1, 0.3, 0.5 and 1 c.c. Two units of complement are used for each different amount of serum, and each

individual amount is controlled for anticomplementary properties. An alcoholic extract of human heart muscle, to which was added 0.2 per cent of cholesterolin, was used as antigen in this technic. Sufficient 0.9 per cent salt solution is added to each tube, so that when the test is complete there will be 4 c.c. in each, for it is for this total amount that the titration for the complement unit is made. One and one-half hours in a water bath at 37° C. is allowed for the fixation of complement, after which the unit of amboceptor and the sheep cells are added, and the final readings are made at one-half hour intervals for two hours. It is to be noted that with the larger amounts of serum the end-reaction is slower in taking place, but with an active amboceptor the final reading can safely be made at the end of two hours. With larger quantities of serum a higher percentage of positive reactions is obtained. With this technic, if the serum is fresh, 1 c.c. is not more anticomplementary than smaller quantities. Normal serum does not cause complement fixation when 1 c.c. is used. The author's investigations corroborate the statement by Lange that in nonsyphilitic cases negative reactions are obtained in the spinal fluid with 10 c.c. A negative reaction with an increased quantity of serum does not positively exclude latent syphilis. In 4 per cent of known syphilitics there was no inhibition of hemolysis when 1 c.c. of serum was used. A Wassermann test made with graded quantities of serum is not only an index of the activity of the syphilitic process, but is of value in indicating the progress of the case under treatment.

CEREBROSPINAL FLUID TESTS, ESPECIALLY THE GOLD REACTIONS IN  
PSYCHIATRIC DIAGNOSIS.—Lawson G. Lowrey, Danvers, Mass.  
*Journal of Nervous and Mental Diseases*, 1917, vol. xlvi, p. 208.

Data are presented covering the spinal tests on the cerebrospinal fluids from 240 cases of mental disease, of which 120 were diagnosed as neurosyphilis. Various methods of performing each test, protein excess, cell count and gold reaction are described, together with a statement of methods now in use. Of 130 positive blood Wassermann tests, 96 occurred in cases of neurosyphilis. Five of 120 neurosyphilis cases gave negative tests. One alcoholic case and one drug case gave positive tests in the fluid. Both of these will probably develop paresis. Ninety cases, or 75 per cent, of neurosyphilis gave positive tests in both fluid and blood. One drug case gave positive tests in both. In 127 counts on the fluids from 120 cases of neurosyphilis, counts below 10 occurred 13 times; 11 to 50, 6 times; 51 to 100, 38 times; above 100, in 30. Counts above 5 per cubic millimeter occurred in 3 arteriosclerotics, 1 alcoholic, 1 manic depressive (postmortem), 3 unclassified organic and 1 traumatic. Excluding bloody fluids, and possibly fluids with old hemorrhages, the globulin tests (Noguchi and Ross-Jones) are positive in

practically all nonsyphilitic cases. The occurrence of slight excesses of albumin in nonsyphilitic organic cases apparently bears out Myerson's contention that the albumin increase is an undifferentiated response. Typically positive gold tests were found in 80 per cent of paresis and taboparesis cases. Atypical positive gold tests were found in 10 per cent of cases; with decidedly atypical tests in the remaining 10 per cent cases. "Positive" gold tests were not found in cases without syphilis, except in old hemorrhage cases. There is close parallelism in the results of all tests considered together. Variations in gold reaction may be due to minor variations in the character of the reagent. These must always be considered. Done under proper conditions and correctly interpreted, the gold reaction is of immense value. It is the sum of the results of all reactions, and not the result of one, which is of value in diagnosis.

**REPORT OF A BRAIN TUMOR IN A CASE CLINICALLY CONSIDERED TO BE PARESIS.**—Lawson G. Lowrey, Danvers, Mass. *Journal of Nervous and Mental Diseases*, 1917, vol. xlv, p. 353.

This paper presents a study of a case of glioma involving the third and posterior portion of the lateral ventricles and the corpus callosum. The case was diagnosed as paresis, but no evidence of paresis was found in the microscopic study of the cortex. The tumor is somewhat unusual in type for its location, as tumors in this region are usually sarcomas or fibromas, while this is a glioma or at most a gliosarcoma. As in many other reported cases of tumors in this region no definite symptom-complex appeared. This case emphasizes the importance of satisfactory spinal fluid examinations in all cases in which paresis is suspected.

**FACTORS IN THE PROGNOSIS OF SYPHILIS OF THE NERVOUS SYSTEM.**—Edward Livingston Hunt, New York City. *Archives of Diagnosis*, April, 1917.

There are five pathologic conditions that appear in syphilis of the nervous system: (1) The involvement of the meninges, (2) the involvement of the arteries, (3) the involvement of the brain substance, (4) the involvement of the cord substance, and (5) syphilis of the peripheral nerves. To reach an intelligent prognosis it is necessary, therefore, to distinguish exactly what particular part of the nervous system is affected, and to what extent. An important point, and one which is not sufficiently thought of, is the strength and persistency displayed by the Wassermann test on both blood and spinal fluid after a certain period of time has elapsed, and after a certain amount of treatment has been tried. Thus it will be seen that a Wassermann, which at the end of six intraspinal injections changes only from a four plus to a three plus, will show less chance of improving than a

Wassermann, which at the end of two or three treatments has changed from a four plus to a two plus. The prognostic value of the Wassermann test is far greater than is that of the cell count. The value of the cell count is almost wholly in diagnosis. No Wassermann examination of the present day is correct unless it is reported in several dilutions. It must be reported in 1 c.c., in .5 c.c., and even .2 c.c. The reason for this is that in certain dilutions the Wassermann is negative, while in others it still remains positive. Therefore, a prognosis of value can not be made until the Wassermann examination has been reported in the smallest possible dilution of the spinal fluid. The clinical examination is another factor. It is well known that the more profound types of syphilis, as a result of treatment, cause few clinical changes. In these cases the pupils and knee-jerks are rarely altered; whereas, in the more superficial and acute types of syphilis, treatment brings about considerable change clinically, as is evidenced by the great improvement which occurs in tremors and speech. Again one must consider the method of administration of other drugs, such as mercury, iodide, and arsenic, but especially mercury. There is no doubt that the administration of mercury by mouth is absolutely useless, and a waste of time. It is also true that the administration of mercury hypodermically, when it results in the formation of hard indurated lumps, is equally useless. Another factor is the information given by both ophthalmoscopic examination which shows a beginning pallor of the optic discs would forecast a different result from one which showed normal discs. A marked increase in blood pressure is important in prognosis. Those cases that have unusually high blood pressure can not stand as radical treatment as those that present a more normal figure; therefore, cases that present an abnormal blood pressure should be a factor of some importance in making prognosis. Consider the condition of the kidney, as illustrated by the urine examination. There is little doubt that a kidney that already shows signs of breaking down will be less favorable for future treatment than one that is normal. Such a kidney will be unable to stand excessive doses of either mercury or arsenic, and will require slower progress, milder dosage, and, therefore, give less brilliant results.

**PARESIS OR DEMENTIA PRECOX?**—Harold I. Gosline, Trenton, N. J.  
Boston Medical and Surgical Journal, 1917, vol. clxxvi, p. 326.

It seems proper that we should call those cases paresis which show the mental picture and the physical signs of paresis, whether they have the positive signs of syphilitic infection or not. It seems to the author that we should call those cases dementia precox which have the mental and objective signs of dementia precox, regardless of whether they have a syphilitic infection or not. For only in this way

can we hope to think and act clearly in the splitting up of the dementia precox group, which seems to be well under way, and only in this way, perhaps, can we solve the question of why certain paretics recover with more dementia than others, why some are less amenable to treatment than others, and, finally, why some have negative findings for lues.

DEATH IN TABES DORSALIS.—MORRIS Grossman, New York. *New York Medical Journal*, 1917, vol. cvi, p. 1030.

The cause of death in tabes is syphilis. Syphilis and tabes lead to death through cardiovascular and renal degeneration and through weakened resistance to nonsyphilitic infections. The probable average age at which death occurs is fifty-three years. The mortality among tabetics over fifty-three years of age is 238 per 1,000. Tabes is as nonlethal as any form of syphilis.

A SIMPLE PAINLESS TECHNIC FOR SALVARSAN INTRAVENOUS ADMINISTRATION.—Charles C. Miller, Chicago. *New York Medical Journal*, 1917, vol. cvi, p. 698.

Simple technic is not alone an advantage to the physician, it encourages patients to submit to these invaluable injections. With the old technic, where the large needles and cumbersome outfits were used, patients have been intimidated, and many who should have several doses of the arsenicals never bring themselves to submit to a second injection.

LUARGOL ("102"), THE NEW REMEDY FOR SYPHILIS.—B. Sherwood-Dunn, Paris, France. *American Journal of Clinical Medicine*, 1917, p. 630.

Luargol is the sulphate of argento-antimoniated dioxydiaminoarsenobenzol; the exact constitutional formula has not as yet been definitely determined, however, owing to its complex nature. The addition of the silver salt to the arsenobenzol adds to the antiseptic properties of the latter. Luargol is to possess the following advantages: (1) The stability of the preparation, which may be kept for several hours, permits of making up a sufficient quantity to treat a large number of patients. (2) The simplicity of the treatment, requiring no complicated apparatus. (3) The benignity of the treatment, which produces only a passing and uncertain reaction and devoid of all grave symptoms or complications. (4) The rapidity of the treatment, in that it calls for only one-day intervals between injections. (5) Its remarkable efficacy, the first, second, and third stages yielding in a few days under the influence of doses much smaller than those needed of salvarsan or neosalvarsan. (6) In 80

out of 100 cases in which had been employed from 1 gram to 1.20 gram of "102," the blood from one to two months after the treatment gave a negative Wassermann reaction.

SALVARSAN AND NEOSALVARSAN MYELITIS: REPORT OF A FATAL CASE.—  
G. W. McCaskey, Fort Wayne, Ind. *Journal of the American Medical Association*, 1917, vol. lxix, p. 1962.

Severe and even fatal myelitis may, though rarely, result from even small doses of salvarsan or neosalvarsan given either intravenously or subdurally. This accident may happen without warning in cases in which the same treatment with identical doses had been well tolerated before. It is not always, if at all, due to faulty manufacture, as the same solution has proved fatal to one and innocuous to others given within the same hour both before and after the fatal dose. Wechselsmann's conclusion that renal block furnishes the explanation of salvarsan fatalities seems entirely untenable. The most plausible hypothesis seems to be the action of toxic compounds in the form of intermediary bodies with especial affinity for the neurons formed in the retrograde changes which occur in the salvarsan compounds and which may vary in different individuals and in the same individual at different times, and of the exact nature of which we are entirely ignorant. Considering the enormous number of these treatments given, the occurrence of myelitis is so rare that it should be ignored as a negligible possibility.

THE MODERN TREATMENT OF SYPHILIS.—Courtney W. Shropshire, and Charles Watterston, Birmingham, Alabama. *Medical Record*, 1917, vol. xcii, p. 767.

The prophylactic treatment is of the utmost importance in syphilis. A dose of salvarsan should be given all patients with lesions on the skin or mucous membranes to destroy the organisms in these lesions, and thereby prevent the spread of the disease. The initial lesion should be removed and the patient treated energetically with salvarsan and mercury consecutively in the primary stage. At least six doses of salvarsan followed by mercury should be given after the Wassermann becomes negative in the secondary and tertiary stage. A positive Wassermann, in the absence of secondary lesions, constitutes the secondary stage of syphilis. An examination of the spinal fluid—Wassermann, globulin cell count, and Lange colloidal test—should be made in every case, if possible, before the patient is dismissed. In the event that any of the above tests are positive, the patient should be treated until the fluid returns to normal.

TREATMENT OF SYPHILIS WITH ARSENOBENZOL POLYCLINIC.—Charles H. J. Barnett, Philadelphia. New York Medical Journal, 1917, vol. cvi, p. 1074.

Arsenobenzol is the best and safest substitute for salvarsan and neosalvarsan. It is nontoxic, whereas every one of the other substitutes, such as arsenobenzol billon (French), or the diarsenol (Canadian) are much more toxic and in some cases more so than even salvarsan. It is best given in 0.4 gram doses, one week apart. The blood should be tested three weeks after the third injection and more injections given according to the result of the Wassermann test. The blood should be tested three weeks after subsequent injections. Injections should be stopped when a negative Wassermann is obtained, and Wassermann tests should be made at monthly intervals for the first six months. If it continues negative after that, tests should be made each three or six months and then each year during the lifetime of the patient and symptoms of the disease watched for.

THE OCCURRENCE AND TREATMENT OF PAIN IN LOCOMOTOR ATAXIA.—Edward Livingston Hunt, New York City. Medical Council, January, 1917.

The most efficacious remedy of all is the intravenous or particularly the intraspinal form of medication. It matters very little whether the drug is salvarsan, neosalvarsan, salvarsanized serum, or bichloride of mercury. Any one of these when injected intraspinaly will give very great relief to tabetic patients who suffer from bladder disturbances, stiffness, and pains in the legs. This form of treatment has been especially of value in relieving the attacks of pain. It is far superior to the administration of drugs by mouth and to the hypodermic use of morphine. It is one not sufficiently recognized and one which ought to be constantly made use of. The dosage of salvarsan or bichloride of mercury should be small at the beginning and gradually increased. The treatments should begin with intravenous injections and later become intraspinal. They should not be given oftener than every ten days or two weeks.

TRUTH ABOUT INTRASPINAL INJECTIONS IN TREATMENT OF SYPHILIS OF NERVOUS SYSTEM.—John A. Fordyce, New York City. Journal of the American Medical Association, 1917, vol. lxix, p. 1487. The article is a reply to Dr. Bernard Sachs' address.

In tabes certain types of cerebrospinal syphilis, as meningitis, meningomyelitis, meningoencephalitis and in optic atrophy with positive findings in the fluid, intraspinal treatment succeeds in re-

lieving or curing the conditions after failure of intravenous and other treatment. It is the only procedure that can be employed after the intravenous treatment fails or when the patient develops an intolerance to arsenic. With proper technic and experience, it is less dangerous than intensive intravenous treatment. In paresis with stigmata of degeneration, the most to be hoped for is temporary arrest of the encephalitis. There are borderline cases of meningo-encephalitis which simulate paresis and which are curable by the treatment in question. The criticism of the method is based largely on the results following imperfect technic and by its employment in cases without clear indications afforded by spinal fluid examination. Aside from these reasons, it has been condemned after short and imperfect trials. In some cases the existing lesions are activated by early injections and cured by persistence in the treatment. The author's statement that it is regrettable that changes in biologic findings should be made the criterion of the efficiency of any therapeutic method is unfortunate from the standpoint of the patient as well as the investigator. With the exceptions noted in the body of the article, there is an intimate relationship between the clinical symptoms and the fluid findings. It is not difficult to select individual cases in which the Wassermann and globulin reactions are unchanged after prolonged treatment; but conclusions based on such exceptional cases are one-sided, unfair, and fail entirely to interpret or correlate the fundamental principles involved. If reliance is placed on clinical improvement alone as a criterion of the action of our remedies and the fluid changes disregarded, few if any, permanent cures will be achieved, and sooner or later the patient's condition will relapse. There is as much reason for basing the efficiency of a therapeutic procedure on the changes in the biology of the fluid as there is in using the blood Wassermann as a test of the value of treatment of syphilis in general. If we were to discard the positive knowledge acquired in the past few years as a result of systematic examination of spinal fluids in syphilis, we should have vague ideas as to the time the fluid is infected, no clear conception of the difference between active and abortive tabes, and no method of differentiating early paresis from conditions that simulate it. Neurasthenic states, headaches, phobias, vague changes in mentality, crises, or impairment in the sexual function are constantly overlooked or wrongly diagnosed by the pure clinician. Arteriosclerosis, chronic alcoholism, and diabetes may cause symptoms easily mistaken for the syphilitic syndrome. The future of the syphilitic individual and the hope of anticipating or arresting the incurable degeneration is largely dependent on early and systematic examination of the spinal fluid.



PROPHYLAXIS IN SYPHILIS OF THE NERVOUS SYSTEM.—Isadore Rosen, New York City. *New York Medical Journal*, 1917, vol. cvi, p. 973.

Since infection of the central nervous system takes place during the early secondary period, the spirochetes remaining dormant for months or years without producing signs or symptoms of a morbid process, it is imperative that a routine lumbar puncture be carried out early in the secondary stage of all syphilitics, if neurologic complications are to be prevented. Spinal puncture properly performed is a harmless procedure and while the headache which follows in so many cases may incapacitate the patient for several days, the discomfort is well worth the information which can only be gleaned from cytobiologic examination. Early and repeated examination of the eyes and nervous system should be made in the case of every patient in order to detect any changes in their inception. Careful serologic observations should be employed as a guide for the indication or contraindication of intraspinal medication. Systematic and intensive treatment, both intravenous and intraspinal, should be administered to patients with a strongly positive spinal fluid. If tabes, paresis, optic atrophy, and other grave conditions are to be prevented, we must interfere early, and by so doing the new school of syphilology, which, with its modern serologic and therapeutic measures, stands for progress and prophylaxis, will soon be looked upon as a great blessing to mankind, notwithstanding the adverse criticisms of some of our colleagues. Every clinic for the treatment of syphilis should have facilities for all the special examinations necessary and an infirmary where the proper therapy can be employed. It should be emphatically insisted upon that no clinic be allowed to treat the disease unless it can comply with the qualifications specified. In this way only can the secondary complications from syphilis be eradicated or reduced to a minimum.

MEASUREMENT OF THE SPINAL PUNCTURE NEEDLE.—A. Levinson, Chicago. *Journal of Laboratory and Clinical Medicine*, 1917, vol. iii, p. 128.

Although it is difficult to establish an exact standard as to the length of the needle in lumbar punctures, it is possible to gain an approximate estimate as to the measurement of the needle in patients of different ages. The author's investigation showed a length varying from 2 to 2.5 cm. in children one year of age; 2.0 to 3.5 cm. in children between one and two years of age; 2.0 to 4.0 cm. in children two to four years old; 2.8 to 4.0 cm. in children four to seven years old, and 3.2 to 4.0 in children 7 to 12 years old. After the age of sixteen, the variation ranged from 4.1 to 10 cm., the greatest number running between 4.5 and 5.8 cm.

## TRADE COMMISSION ACTS ON SALVARSAN PATENT

Nov. 27, 1917, the Federal Trade Commission entered orders for licenses to three firms to manufacture and sell the product heretofore known under the trade names of "Salvarsan," "606," "Arsenobenzol," "Arsaminol," patent rights which have been held by German subjects. The orders for licenses are subject to acceptance and agreement by the licensees to the stipulations made by the Commission. Upon such acceptance and agreement, licenses Nos. 1, 2, and 3, will be formally granted by Secretary L. L. Bracken, acting for the Commission.

Hereafter, this important drug will be manufactured and sold under the name of "ARSPHENAMINE."

The Trade Commission's action was taken under Section 10 of the Trading With the Enemy Act under direction of Commissioner Fort, upon recommendation of C. H. McDonald, Edward S. Rogers, and Francis Phelps, in charge of granting such licenses. The Public Health Service has prepared rules and standards for the manufacture and testing of "Arsphenamine" and will supervise its manufacture, authority having been conferred on the Public Health Service by the Secretary of the Treasury, and the observance of the rules and standards become a condition of the license.

The three firms which will be hereby permitted to manufacture and sell "Arsphenamine" are Dermatological Research Laboratories, of Philadelphia; Takamine Laboratory, Inc., of New York, and Farbwerke Hoechst Company (Herman A. Metz Laboratory), of New York. The original patent for manufacture of what has heretofore been known as "Salvarsan," etc., was issued to Paul Ehrlich and Alfred Bertheim, German subjects and assigned to Farbwerke Vormal's Meister, Lucius and Bruning of Hoechst on the Main, Germany.

The supply of the drug now licensed to be made in America, up to 1915, was almost exclusively obtained by importation from Germany. It is at present the only known specific for virulent blood poison. From the outbreak of the war importation became more difficult.

Before the war began, the patented drug was sold at \$4.00 per dose, which is approximately \$3,500 per pound, and speculatively it

has brought as high as \$35.00 per dose. While the price of the product is not fixed at this time by the Commission, the right to fix prices is retained, and a price of \$1.00 per dose to the Army and Navy, \$1.25 per dose for hospitals, and \$1.50 per dose for physicians, are the prices at which some, at least, of the licenses have stated that they intend to offer the licensed drug.

The enormous shortage of supply on this important product will immediately be relieved, and the article placed in the hands of the Government, the hospitals and the medical profession at a price lower than ever before.

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#### A CORRECTION

TO THE EDITOR:—In my paper appearing in the October, 1917, issue of the JOURNAL, entitled: "The Technic of the Complement-Fixation Test for Syphilis," wherever the strength of the salt solution is stated it is erroneously stated as 85% or (85%) instead of .85% or (.85%); and upon page 817, the temperature for inactivation of the blood serum is erroneously stated as 37° C. instead of 56° C.

As it was impossible for me to correct the proof of this article, owing to reasons known to the editor, these mistakes occurred; and it is requested that this correction be published in the next issue of the JOURNAL.

CHARLES F. CRAIG,  
Lieut.-Col., Medical Corps, U. S. Army.

## VALUABLE SUGGESTIONS FOR CONTRIBUTORS TO THE AMERICAN JOURNAL OF SYPHILIS

"The four rules for the preparation of an article will then be: (1) Have something to say; (2) Say it; (3) Stop as soon as you have said it; (4) Give the paper a proper title."<sup>1</sup>

Let your phraseology express one meaning and one only. Be clear.<sup>2</sup>

**Manuscript.**—Manuscripts should be typewritten, with wide margins, and double spaced, on one side of paper 8½ by 11 inches in size. The original copy should be sent to the "Journal" and the carbon copy retained by the author. Number the leaves consecutively, beginning with the title page. Put your name and address on the manuscript.

**Illustrations.**—Illustrations should be clear, preferably pen-and-ink drawings. Of photographs send a good print rather than a negative. Have lettering parallel to the bottom and top margins, and of sufficient size to be clear if cut is to be reduced. Tracings should be in black-and-white; avoid colors. Write your name on back of each picture; number them in one series (Fig. 1, etc.) to the end, and indicate in margin of the manuscript about where each is to be printed. See that the text references and "figures" correspond. Legends for illustrations should be written on a separate sheet.<sup>3</sup>

**Bibliographic References.**—Give only references actually consulted. If an article is known only through an abstract give reference to the abstract in addition to that of the source. References are printed to be of help in further reading; therefore they must be complete, concise, and correct. Follow the style of the "Index Medicus" and "Index-Catalog of the Library of the Surgeon-General's Office." Be conservative in the use of abbreviations.<sup>4</sup>

**Arrangement.**—As authors are quoted in the text give each a number in the order of citation, and number the bibliographic reference with the same number. Arrange the references in a list at the end of the article in the order of the numbers (see below), or arrange items in alphabetical order according to last names of authors, and distinguish between articles by the same author by the use of the date after his name in the text.

**Foot-notes.**—Where an author wishes to use foot-notes at bottom of each page instead of the bibliography at end of article, the foot-notes should be written in the text, but separated from it by horizontal lines above and below, or *better*, place them at bottom of each page. Use figures to indicate these foot-notes, and number consecutively (1, 2, 3, etc.) throughout the article. If in addition to the bibliography mentioned above it is desired to use foot-notes on certain pages, these can be indicated by an asterisk (\*).

**Final Reading.**—Let some one other than the author read the manuscript with these directions in mind.

**Shipment.**—Send manuscript flat, postage paid, to the associate-editor, Dr. Wm. H. Deaderick, Dugan-Stuart Building, Hot Springs, Arkansas.

**Proof-reading.**—Read carefully, with special attention to spelling of names and bibliographic data. Make corrections *in the margin* only with lines drawn from the revision to the point of change in the text. Answer queries in the proof by making correction or crossing out the query. Verify your references from the sources, not from your carbon copy.

### References. (Read these.)

<sup>1</sup>Billings, J. S.: Our Medical Literature, Trans. VII Intern. Med. Congress, Lond., 1881, i, 54-70.

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<sup>3</sup>Suggestions to Medical Authors, issued by the A. M. A. Press, Chic., A. M. A., [1914 (?)].

<sup>4</sup>Place, F.: Bibliographic Style in Medical Literature, Med. Record, N. Y., 1913, lxxxiii, 157-160.

# The American Journal of Syphilis

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## Original Articles

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### SYPHILIS OF THE STOMACH: A REPORT OF FORTY CASES IN WHICH THERE WERE DEMONSTRABLE LESIONS AND THERAPEUTIC CURE OR IMPROVEMENT\*

By G. B. EUSTERMAN, M.D.

*From Mayo Clinic, Rochester, Minnesota*

(Received for publication, March 21, 1918)

A RENEWED and growing scientific interest, a gradual increase in our knowledge, and a certain amount of controversy and skepticism, are centered about visceral syphilis and particularly about one of its interesting forms, gastric syphilis. To the internist this phase of the condition should make a peculiar appeal because of the rarity, the difficulty of recognition and satisfactory diagnosis, the problems arising in differential diagnosis, and because the management of the disease lies almost entirely within the domain of medicine and is so frequently attended by brilliant therapeutic results.

No other problem in internal medicine, in my experience, seems to require more careful scrutiny and judgment, or closer consideration of all data. Enthusiasm, on the one hand, may influence one to accept or report that which has not been satisfactorily proved, while undue conservatism or a lack of clinical foresight may cause one to reject or

overlook that which is, or eventually proves to be, a specific lesion. Certain inherent characteristics explain or give rise to clinical uncertainties but these are readily outweighed by the fascination the observer experiences when in the actual presence of this most protean and ubiquitous of all human diseases. And surely syphilis in all its manifestations and relations to abdominal visceral disease commands our unusual interest.

I shall review briefly the essential pathologic anatomy. The gross gastric lesion is a tertiary, usually late, manifestation of the disease, both in the hereditary and in the acquired form. It is the result of a circumscribed or diffuse gummatous infiltration of variable extent, a chronic productive inflammatory process, usually having its origin in the submucosa. This process may involve any or all the structures of the organ but having a predilection for the pars pylorica, it often extends well upward along the lesser curvature, and to a lesser degree involves the greater curvature. Syphilitic ulcer, often multiple, is the expression of a broken-down gumma involving the mucosa and submucosa, or, it may occasionally arise as the result of an obliterating endoarteritis. The sequelæ invariably are scar tissue from cicatrization, with or without stenosis or hourglass deformity and fibrosis due to dense connective-tissue formation, resulting invariably in a deformed, contracted, thickened organ in advanced, untreated cases. Profuse hemorrhage, perforation or fistulous formation are of rarer occurrence than in the benign ulcer cases, but a hyperplastic chronic perigastritis is relatively more common. Gummata, like benign ulcers, may heal spontaneously, leaving scars or deformity of variable degree. In addition to these gross changes there is considerable pathologic evidence to prove the existence of a syphilitic gastric catarrh, which may be a manifestation of the secondary or tertiary stage, the direct or indirect result of the infection. Thus, symptomatically and anatomically, specific gastric disease may simulate benign chronic catarrhal gastritis, ulcer and its sequelæ, fibromatosis, scirrhus carcinoma and tuberculosis of the stomach. But from the therapeutic standpoint the difference is striking. To the experienced clinician, roentgenologist, and surgeon, there are certain extrinsic and intrinsic factors, not pathognomonic, but highly suggestive of specific disease. These differ from the usual characteristics of the other conditions noted, and have an invariable differential diagnostic value.

The proper interpretation of the sources underlying gastric disturbances in syphilitic suspects or in proved tertiary syphilitics may give rise to some difficulty, and in my study of a considerable amount of material, numerous questions have presented themselves.

A large majority of syphilitics make no complaint of gastric malfunction. Observations in this respect by various authorities show similar findings. McNeil in a review of 1,200 clinical syphilitics states that only 97, or about 8 per cent, complained of some more or less serious forms of gastric disease, among which there were only 2 cases of organic syphilis. White reports that of a group of 600 syphilitics with strongly positive Wassermann reactions (excluding those with hepatic cirrhosis, lues hepatica, nephritis and tabes) 44 (7.3 per cent) had prominent gastric symptoms. In 35 cases no definite lesion of the stomach was proved; in 9, actual luetic or coincident lesions were found (ulcer, gumma or cancer). It is readily apparent that a variable combination of factors in the group of syphilitics having gastric disturbances may give rise to considerable speculation and to diagnostic difficulties when taken in conjunction with the results of specific therapy. To avoid confusion and for practicable considerations the discussion in this paper will be confined to the demonstrable gastric lesions.

There are various factors that enter into the determination of the specific nature of a gastric lesion. By conforming to the requirements laid down by Chase, it would seem that many of the doubtful cases could be readily excluded. These requirements are: (1) Positive Wassermann reaction, (2) evidence of syphilis elsewhere in the body, (3) demonstration of a lesion in the stomach by the roentgen ray, and (4) therapeutic improvement.

#### POSITIVE WASSERMANN REACTION

Obviously, it will be seen that there may be instances of gastric syphilis without a consistent positive Wassermann reaction having been procured, at least not on the first attempt. It is a common experience to find, for example, definite evidence of cutaneous syphilis in which the reaction was not obtainable but in which there was a history of a primary lesion or exposure and therapeutic cure.

The provocative Wassermann test has helped us definitely in three of our cases. The test seems clinically inapplicable, however, owing to the amount of labor involved. After a study of 103 provocative tests,

Stokes is of the opinion that it is of the least service of any of the diagnostic tests in active, deep-seated visceral, osseous, and central nervous system syphilis. The sensible conclusion is that clinical judgment and the therapeutic test are superior to this procedure in the diagnosis of obscure cases.

#### EVIDENCE OF SYPHILIS ELSEWHERE IN THE BODY

It is sometimes difficult to obtain additional evidence of syphilis, but by painstaking, systematized search, and by having in mind all the various manifestations of the disease, we frequently find evidence of the existence of syphilis elsewhere.

#### DEMONSTRATION OF A LESION IN THE STOMACH BY THE ROENTGEN RAY

From my own experience, all gross syphilitic lesions could be easily demonstrated on the roentgen plate, and this is one of the requirements with which we are most readily able to conform. It is quite obvious, however, that small areas of gummatous involvement, or cases of single or multiple shallow ulcers, characteristic of the syphilitic type, and all cases of syphilitic gastritis especially, may easily escape detection.

#### THERAPEUTIC IMPROVEMENT

Practically all syphilitics show prompt improvement clinically under adequate treatment whether or not they actually have a gastric lesion, but structural improvement in the stomach itself would argue strongly for the true specific nature of the trouble. Thus all the requirements may not be definitely fulfilled or the results may even go beyond the bounds of these requirements, and the condition still be essentially specific. In our later series (eighteen or twenty cases) these requirements were easily met.

Bearing in mind the foregoing, one has a fairly definite working criterion on which to prove or disprove the specificity of the lesion co-existing with syphilis. Benign or malignant gastric lesions may obtain as readily in the syphilitic as in any other type of individual and the proof or disproof of the syphilitic nature of the lesion under these circumstances would seem to depend largely on the degree of response to adequate antisppecific treatment or, if possible, on the histologic examination of the tissue resected. There seems to be a lack of direct evidence to show that a syphilitic gastric lesion ever assumes a malig-





Fig. 1.—(173711). Syphilitic hourglass with obstruction. Female, age 38; probably heredosyphilis. Gastric symptoms fourteen months, pain and emesis, achylia. Wassermann + + +. Marked improvement after prolonged course of treatment. Gain 40 pounds. Recovery not complete, probably because of the obstruction present. No reray. Operation may be necessary. The illustration shows a markedly dilated esophagus; this type is most characteristic of the roentgen appearance of gastric syphilis.



nant form or that a benign ulcer becomes gummatous in the presence of systemic syphilis.

Among the questions that naturally arise are: What proportion of round ulcers, so-called, classified as benign calloused ulcers are actually syphilitic in origin? And what role may the symptomatology, and the gastric chemistry in combination with results of serologic examination, play in their recognition? The same question may be raised with respect to duodenal lesions. In such cases, Neumann has reported cases found at necropsy, of duodenal ulceration and yet the same author stated that probably 20 per cent of all round ulcers were syphilitic in origin, a statement with which we can not agree. Mortimer has recently reported a fairly reliable instance of duodenal syphilis. Our experience prompts me to state that syphilis is a negligible factor in simple, uncomplicated gastric or duodenal ulcer, especially when associated with hyperacid gastric contents and the generally accepted syndrome of benign ulcer, with the possible exclusion of circumscribed syphilitic ulceration and stenosis of the pylorus. Simple ulcers associated with achylia or subacid values may have specific etiologic significance. It is to be remembered that the roentgen demonstration of a lesion is anatomic and not etiologic. The incidence or history of syphilitic disease or the finding of positive Wassermann reactions or other evidences of syphilis in ulcer-bearing patients as we see them, is exceedingly rare, occurring in about one-third of 1 per cent. Such lesions undergoing intensive antispecific treatment are invariably uninfluenced, with a consequent indifferent influence on the gastric disturbance. In instances of gastric cancer the differentiation from syphilitic lesions is made with greater difficulty and uncertainty. In a careful perusal of the literature and with frequent misgivings in regard to our own cases, I have been impressed with the frequency with which ulcers have been excised or other surgical procedures carried out, or with which gastrectomies have been performed for supposed cancer when the specific nature of the lesion was probably never discovered or thought of as a possibility.

Pathologists still consider syphilis of the stomach as more or less of a curiosity. In a review of the literature I found that only a dozen or more of the cases clinically diagnosed syphilis of the stomach have been verified by histologic examination. The meager results in

necropsies performed on subjects with late acquired or congenital syphilis, for example, those by Chiari, Stolper, and others, and more recently by Symmers in this country, seem to warrant their conclusions. Symmers, after finding only one ulcer of indubitably syphilitic origin in 314 necropsies, states that unless the diagnosis of gastric syphilis is confirmed by microscopic examination he is not inclined to accept it. For scientific reasons it is to be regretted that all fairly authentic cases of gastric syphilis do not come to necropsy, but fortunately when such cases are recognized the condition responds so favorably to treatment that postmortem evidence is not available. The number of reported cases which have been diagnosed clinically is approximately 200. It would seem that a considerable number of the earlier cases and some of the recent ones can not in the light of our present knowledge be accepted as definite instances of organic gastric syphilis because they have been incompletely studied.

The era of serology and roentgenology has naturally given an impetus to renewed interest in and to more reliable insight into these obscure conditions, and has made numerous reliable case reports possible. Serology and roentgenology are useful diagnostic agents which have furnished data necessary to conclusive clinical diagnosis, the disquieting attitude of the pathologist notwithstanding. After all, the discrepancies between the attitude of the pathologist and that of the clinician may be more apparent than real. If the case reports not adequately proved are excluded, and if we recall the universal distribution of syphilis and its incidence,—from 10 to 15 per cent alone of the urban population of Europe being infected,—it will be seen that the number of case reports is not large even though the incidence of organic gastric disease in such cases is remarkably small. In view of this I do not feel that we have any apology to offer for having thus far recorded only forty authentic instances of the disease during an investigation of more than 6,000 proved cases of ulcer and cancer of the stomach, and exclusive of several thousand other cases in which the clinical diagnosis of a gastric lesion was established beyond cavil. In all probability numerous other instances of luetic involvement have been overlooked.

While it is apparent that ultimate diagnosis depends on the demonstration of spirochetes microscopically in the exsected tissue, yet the grouping with all the evidence from all sources may maintain a diag-



Fig. 2.—(214887). Luetic hourglass stomach. Male, age 34. Primary lesion twelve years previously; gastric disturbances for  $1\frac{1}{2}$  years. Pain, vomiting, nocturnal pain, a few mouthfuls causing fullness. Achylia. No retention. Wassermann ---. Following intensive antisyphilitic treatment patient gained 10 pounds, eats all solids, shows marked clinical improvement. Reray three months later. No anatomic improvement.



nosis as conclusively as many others which are freely accepted. After all, there is no decisive ultimate diagnosis, particularly in the cases of acquired syphilis, because up to the present time spirochetes have not been demonstrated in the gastric tissue and we know that the histopathologic criteria are not conclusive.

Without going into statistical details, which are always tiresome and easily forgotten, I will simply call attention to the more tangible data and deductions arrived at in a study of 40 cases in 12 of which the patients came to operation. There were 29 males, the average age being 37 years; and 11 females, the average age 35 years. Total average 36 years. All the women were married, and 3 admitted they were or had been prostitutes. The primary lesion was a genital chancre in all the cases that could be determined, except in four instances; two of these infections occurred in surgeons and represented an innocent infection of the finger; 2 others were cases of heredosyphilis. Wassermann tests were made in 35 cases; the remaining 5 cases antedated the routine use of the test, but were verified by surgical exploration and postoperative therapeutic management. Thirty-one of these 35 cases gave strong reactions. Four reacted later or the reaction was obtained by the provocative method, and in one the reaction never became positive. Six of the 31 patients with initial positive Wassermann reactions denied any luetic infection. The average duration of symptoms was a little more than two years. The earliest period of onset of symptoms after infection was one year, the latest twenty-eight years. The average period was twelve years. In syphilitic aortitis the average period of the onset of symptoms after infection is about eighteen years. Thus it appears that the age incidence is of the greatest significance averaging quite regularly 36 years, in contrast with the age incidence in ulcer, which is about 45 years, and in cancer which is 54 years. This average seems quite out of proportion to the extent of the pathology invariably present. Finally, symptoms develop on an average of twelve years after infection, which makes the average age of the patient about 23 or 24 years at the time of the infection. These figures seem in keeping with the general age incidence in syphilis.

In the physical examination in the obstructing hourglass cases, the patients were generally undernourished and about half of them were anemic but not cachectic. The objective evidence of syphilis

elsewhere was routinely sought for and positive findings were made in proportion to the acumen of the general diagnostician.

In a series of twenty-three cases which I<sup>4</sup> reported several years ago I had noted the association of aortitis, aortic endocarditis, aneurysm, gummata of the liver or syphilitic cirrhosis, involvement of the spleen, cutaneous lesions, gummatous meningitis, etc., in about one-third of these cases. In the last seventeen cases of the present series (40 cases) observed, more careful scrutiny showed greater incidence of other signs of syphilis, singly or in combination. They were recorded as follows:

Enlargement of the lymphatic glands, usually general in distribution, especially those involving the postcervical and epitrochlear nodes, occurred in 10 cases. In one case an abdominal mass, regarded as gummata or hyperplasia of the mesenteric lymphatics, was discovered as this enlargement disappeared under treatment. Next in order were evidences of involvement of the central nervous system. Irregular or unequal pupils were recorded in 6 cases, disturbances of the pupillary reflexes in 2, frank tabes in one, internal ear deafness in 2, and disturbances of the superficial reflexes in 2. In the cutaneous system a papillary eruption was recorded in one case, healed lesions or scars in 3, genital scars in 4, a venereal wart of the prepuce in one. Defect, perforation and crusting were noted in the nasopharynx in 4 cases and saddle-nose in one. Tibial periostitis was recorded in one case, splenic or liver involvement in 4 cases. The cardiovascular system objectively was intact in all of these cases.

#### SYMPTOMATOLOGY

In a careful and detailed review of the case histories the classification would seem to depend most logically on the extent and site of involvement, and we have therefore, naturally grouped them under such classification in three groups:

1. Cases in which there are circumscribed pyloric lesions associated with normal or subacid values with or without stenosis.
2. Cases in which there are fairly circumscribed lesions irrespective of the site, associated with achylia.
3. Extensive lesions with hourglass deformity or general marked contracture or cirrhotic stomach, usually associated with achylia.

The cases in the first group simulate closely benign lesions at the





Fig. 3.—(203121.) Syphilitic obstructing gumma of the pylorus. Male, age 41. Primary lesion seventeen years previously, gastric symptoms of two years' duration, progressive. Pain, loss in weight, strength and appetite. Gnawing, empty feeling, and burning sensation passing upward into throat three to four hours after meals. Food, alkali, and postural ease, occasional emesis of food residues soon after meals. Continuous type with brief remissions. Total acids 36, free HCl 20. Moderate food residues. Operation Aug. 4, 1917—resection  $4\frac{1}{2}$  inches of the pyloric end of the stomach. Gummatous tumor with multiple shallow ulcers on the mucous membrane side. Postoperative Wassermann reaction positive. Patient admitted lues which was denied previously. Several courses of mercurial inunctions. Marked improvement, clinically cured—gain of 20 pounds.



pylorus. Owing to the intermittent course of the disease at the outset the characteristics, delayed pain and distress following alimentation, are controlled wholly or in part by alkalies, foods, liquids, posture, etc., and differ from benign lesions in that the course is more rapidly progressive. The relief afforded by food, alkalies, etc., soon disappears. The onset of pain is quite promptly after meals in the later course, and the symptoms then do not respond to treatment by ordinary methods of diet and medication.

In the cases in the second group, characterized by lesions not extensive and by associated achylia, the symptoms are not exactly like those of either ulcer or carcinoma. The onset of pain is usually promptly after meals and the other associated symptoms simulate those of chronic catarrhal gastritis.

In the third group of cases in which there is extensive involvement or hourglass deformity or both, the symptoms are variable. They are usually the result of mechanical factors; that is, the introduction of food promptly occasions distress owing to a markedly reduced capacity. The condition is characterized by a feeling of fullness, sometimes a bursting sensation, and such patients immediately attempt to vomit in order to relieve themselves. Anything which removes the gastric contents affords relief. The high hourglass stomach may merely regurgitate, as in patients with obstructions high in the pars cardiaca or in the lower esophagus. In two such cases the patients did not complain of any pain, they merely regurgitated. Still other disease conditions simulate the clinical picture of this group, for example, scirrhus carcinoma of the stomach, dyspepsia associated with gall-bladder disease, or gastric disturbances associated with certain fevers. Roentgenologic evidence of marked gastric pathology present in an adult, between the third and fourth decades of life, and the absence of cachexia, strongly suggest the possibility of syphilis.

Pain was present in 39 of the 40 cases and was characterized as severe in 10. The favorite method of relief was by vomiting in 32 cases (82.5 per cent). Pain appeared immediately or fairly promptly after eating in 26 cases (65 per cent); it was constant in 8 (20 per cent); at some variable time after meals in 5 (12.5 per cent). While nocturnal pain is commonly regarded as a frequent characteristic of syphilitic lesions, benign gastric lesions with supersecretion or stasis will frequently have this characteristic; but in gastric lesions asso-

ciated with achylia the nocturnal pain may point to a luetic origin. However, this is not a feature on which we place much diagnostic significance. Hemorrhage is comparatively rare, being recorded in only two instances (5 per cent); emesis, nausea and flatulency were the chief symptoms, next to pain. Quite contrary to all malignant lesions of the stomach which gastric syphilis simulates in chemical and roentgenologic characteristics, the appetite was noted as about normal in 49 per cent and ravenous in 7.5 per cent of the cases. In other words, more than fifty-five of the patients had normal or increased appetite. Complete absence of appetite was recorded in 12.5 per cent. The average loss of weight was 35 pounds; 50 per cent had lost from 40 to 75 pounds. Patients with multiple hourglass stomach or marked cirrhosis, especially the hereditary type, showed an extreme grade of malnutrition.

In the examination of the gastric contents the number of patients without free acid or ferments was 32 (80 per cent). Those with free hydrochloric acid were 18 (20 per cent). The number with achylia alternating with free hydrochloric acid was 3 (7.5 per cent). In one there was a return of free hydrochloric acid after intensive treatment. Thus unquestionably, with the exception of cases of obstructing circumscribed lesions at the pylorus, practically all cases of gastric syphilis are associated with achylia or rarely with subacid values. This is an important fact to be always borne in mind and it is verified by authentic recent case reports as well as by observers who have carefully searched the literature for reports of authentic cases in which the gastric chemism was given particular attention. The absence of free acid in these nonobstructed cases is partly due to mechanical factors and to the influence, local as well as systemic, of the infection on the gastric mucous membrane. In those cases of actual specific gastric lesions, indirect influences involving the pancreas, the liver and the system generally also play a part.

#### PATHOLOGY

In view of the short duration of the disease, averaging a trifle more than two years, the changes that take place in the stomach are extensive. Such changes seem to be dependent more directly on the duration of the infection than on the duration of the symptoms of gastric malfunction. Cases in the exudative stage may show extensive infil-



Fig. 4.—(145508). Extensive syphilitic cirrhosis and contractures involving chiefly the middle and lower third. Heredoseyphilis. Male, age 25. Wassermann negative. Gastric disturbances 7 years. Discomfort after eating small amounts of solid foods. Regurgitation, exploratory operation three years previously. Numerous stigmata. moderate symptomatic improvement following antisyphilitic treatment.



tration that will clear up completely under treatment if the condition is recognized and treatment instituted in time. Much may be conjectured as to the pathogenesis of the condition in view of the disproportion between the duration of the clinical symptoms and the pathology. Twelve of the 40 patients as has been stated, were operated on and all showed extensive involvement. The stomach was deformed or was shrunk and thickened. Hourglass deformity was noted in 4 instances (Figs. 1 and 2); a pyloric mass exhibiting multiple shallow, dirty, ulcers on the mucous membrane side was recorded in 5 (Fig. 3); obstruction was present in 3, and extensive general involvement classified as cirrhosis was noted in 3 (Fig. 4). In the cases not operated on (28) the roentgenograms had to be depended on for the location and extent of the involvement. These are fairly faithful, but, of course, the disease process is, on the average, one-third more extensive than is apparent from examination of the roentgen plates. In these 28 cases the pylorus was involved in 10, and the pylorus and media in 5. In all the patients operated on, the pylorus chiefly was involved in 20 (50 per cent). Hourglass contraction was recorded in 5, and in several of these the pyloric area was involved in the deformity. The pars media and cardiaca, representing the upper third of the stomach, were involved in 3, the cardia alone in 1 (Fig. 5), and there was a general diffuse syphilitic cirrhosis in 4; a total of 7 of the entire series.

It will be seen that in order and frequency the involvement chiefly concerned the lower third of the stomach; next in order the media, including those cases of hourglass which are usually found in the upper or middle third, and, finally, the general marked involvement of the cirrhosis cases; the rarest form is that in which the pars cardiaca alone is involved.

From the roentgenologist's standpoint my colleague, Dr. Carman, in a careful survey of the material herein reported, deduces the following as quite characteristic of gastric syphilis:

1. Filling defect of the gastric outline, usually without corresponding palpable mass.
2. Shrinkage of gastric capacity.
3. Stiffening and lessened pliability of the gastric wall.
4. Absence of peristalsis from the involved area.
5. Pylorus gaping rather than obstructed.

6. Six hour retention less common than in other gastric lesions (23 per cent).

7. So-called hourglass stomach; upper loculus expanded and bulbous, lower loculus tubular, due to extensive irregular concentric contraction.

8. Patient usually under cancer age and not ill in proportion to the extent of disease shown by the x-ray.

One can see the significance of such roentgenologic data in combination with the results of serologic examination or other clinical evidence of syphilis, irrespective of the clinical syndrome which seems still generally unrecognized, or not entirely clarified, but which will prove to be a fairly applicable working factor in the diagnosis.

The antisyphilitic management of all these cases was fairly intensive, depending somewhat on the degree of response to the Wasserman test. In the initial treatment the patients received at least six intravenous injections of salvarsan, neosalvarsan or arsenobenzol at intervals of a week. During and subsequent to this period from twenty-one to thirty-six injections of a soluble salt of mercury were given intramuscularly or a course of vigorous mercurial inunctions was applied. A repetition of this treatment was carried out either at the clinic or under direction of the local physician. The end results are encouraging. Of the series of 40 patients, 38 were heard from. Those clinically cured were 16 (42 per cent). Those regarding themselves as improved were 19 (50 per cent), or a total of 92 per cent. Three stated that they were not improved, representing a failure of 8 per cent. Twenty-two of the patients were re-examined, including a re-ray, and of these 8 (36.6 per cent) were anatomically improved. Several underwent a total anatomical cure. We feel that this percentage could be increased considerably if all the patients had been re-examined, but many of them live at a considerable distance, and, being clinically improved, have had no incentive to return for further treatment or study.

In concluding it seems logical to consider those factors which give rise to the suspicion of syphilis of the stomach and to summarize briefly the salient features that go to establish the identity of the disease. Obviously, all dyspeptics with a definite history of primary or secondary lesions, or a suspicious genital sore of any description, or repeated gonorrheal infection, would arouse the suspicion that the





Fig. 5.—(208425.) Syphilis of the pars cardiaca, rare form, easily mistaken for carcinoma. Patient, male, age 33. Primary lesions twelve years previously, gastric disturbances 1½ years. Distress after food in epigastrium. Six months ago onset of emesis after all food except milk and small amounts of milk toast. Wassermann ---- (9 20 17). Roentgen ray diagnosis: inoperable carcinoma of the stomach. Filling defect cardia. Intensive course of treatment here with marked improvement. Gained 17 pounds. Ravenous appetite. Wassermann negative 10 20 17. Roentgen ray 11 5 17. Condition shows marked anatomic improvement. To date patient is clinically cured. He reports that he is feeling fine with no gastric symptoms whatsoever.



disturbance might have its origin in syphilis. This is true in married persons whose union is childless or marked by spontaneous abortions, miscarriages, or premature or still births; in patients, usually young adults, exhibiting signs of heredosyphilis; in all cases of gastric malfunction in which there are objective signs of syphilis in the absence of an infection; in all atypical gastric disturbances; and in all cases in which response to the usual dietetic and medical management is inadequate. In developing a history of syphilitic infection, the greatest difficulty is encountered in the female patients, the majority of whom often remain in ignorance of the exposure or the nature of the infection when present. A composite clinical picture may be constructed as follows:

The patient is an adult, averaging 35 years of age. The gastric disturbance is, on the average, of a little more than two years' duration, characterized chiefly by pain, vomiting and flatulency coming on fairly promptly after taking food. The course is progressive, with gastric chemism and roentgen findings, rather that of carcinoma. The patient is undernourished but not cachectic, may be somewhat anemic, and there is usually absence of any palpable gastric mass. The gastric lesion is invariably extensive, is occasionally localized in the pyloric area, with only a slight tendency to produce stenosis. Such characteristics, in conjunction with a positive Wassermann reaction or with a history of infection and other clinical signs of syphilis, are strong presumptive evidences of specific gastric disease.

Bearing these characteristics in mind and that which further proves their reliability, the disclosures of the fluoroscope and roentgenogram in combination with the results of gastric analysis or the demonstration by the surgeon of a fairly extensive ulcerating mass in a more or less generally involved stomach, especially in an adult between the third and fourth decades, has in numerous instances uncovered a specific history previously concealed, or has pointed out the necessity for serologic examination. In other words, the diagnosis of systemic and visceral syphilis has been worked out backward, insofar as gastric syphilis is concerned, by the employment of reliable proved diagnostic data.

#### SUMMARY

1. Organic gastric syphilis is rare even in advanced cases. The average age incidence was between 35 and 40 years, the average dura-

tion of the symptoms about two years and the average duration of the infection about twelve years.

2. Exclusive of the congenital cases and the advanced obstructing hourglass types, cachexia was rare, anemia was not marked and there was an invariable absence of gastric tumor.

3. The syndrome was not characteristic but was usually variable, depending largely on the site and extent of the involvement. The localized gummata of the pylorus with or without stenosis and with free hydrochloric acid in the gastric extract simulate benign pyloric ulcer; in obstructing high hourglass, the patients usually have considerable pain and vomiting soon after taking food; in the contracted and deformed types there is distress, pain and associated symptoms in proportion to the nature and amount of the food taken. The symptoms in the main closely approach those characteristic of a slowly progressive form of scirrhus carcinoma. The symptoms common to all the cases were: A fairly marked progressive course, prominence of pain soon after eating, invariably associated with nausea and vomiting, the absence of hemorrhage, maintenance of appetite in the majority of cases and marked loss of weight without definite cachexia.

4. Achylia was present in over 80 per cent of the cases; in 20 per cent there was free hydrochloric acid in the gastric extract but usually with subnormal values. In  $7\frac{1}{2}$  per cent of the latter achylia alternated with free hydrochloric acid secretion.

5. The pathologic anatomic process was a gummatous infiltration, diffuse or circumscribed. Syphilitic ulceration of the mucous membrane was usually a secondary phenomenon. There was a predilection for the pylorus and media and extension upward along the lesser curvature. Hourglass contractures usually involved the pars media. Pyloric stenosis is more infrequent than in benign ulcer and malignant conditions, approximately 20 per cent. Gastric involvement was usually extensive even when the symptoms were of brief duration. General diffuse syphilitic cirrhosis was characteristic of the congenital cases. In advanced cases hourglass contracture, marked thickening, deformity and contracture due to fibrosis was the rule.

6. Intensive antisypilitic treatment in the early stages may produce actual clinical and anatomic cure. In advanced cases there may be little or no response. This series showed clinical cure in 42 per cent and improvement in 50 per cent, representing a total of 92

per cent improved or cured. (This includes twelve patients, 30 per cent of the cases, which required surgical interference.) Treatment had no influence in 8 per cent. Of the patients re-examined, 36.6 per cent showed anatomic improvement, three having complete anatomic cure.

7. The proof of the specificity of a lesion involves numerous factors. Differential diagnosis is often exceedingly difficult. The requisites are: Demonstrable evidence of a gastric lesion, positive Wassermann reaction or other reliable evidence of syphilis elsewhere in the body, or both, and definite, sustained therapeutic improvement. These factors in conjunction with achylia or subacidity in the majority of cases, with the roentgenologic characteristics herein described, in addition to anatomic improvement or cure, seem to make the clinical or intra vitam diagnosis of syphilis of the stomach conclusive.

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## SYPHILIS AT THE PYLORIC SPHINCTER OF THE STOMACH

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UP to 1907, when Henri Pater collected and analyzed all cases of syphilis of the stomach, he recognized only two as authentic, the one of Hemmeter and the one he saw with Hayem, where the syphilitic process involved the pyloric sphincter. Of late years, many cases of syphilis of the stomach have also been examined by the x-rays and some of these operated upon (LeWald, Downes, Carman), but only very few of these were situated at the pyloric sphincter. Therefore, I feel justified in adding one more case, especially as it was operated upon twice and both times believed to be cancer, just like Hayem's case, until the microscopic examination of the resected portion showed it to be syphilitic. The case with its clinical, serologic, roentgenologic and microscopic findings was presented for its rarity on Dec. 6, 1917, at the meeting of the German Medical Society of Chicago, and was fully discussed. Especially the microscopic sections were accepted as showing true syphilitic lesions, although the *treponema pallida* was not demonstrated.

What I believe lends a special interest to this case is the careful roentgenologic examination which demonstrated the correct seat and extent of the lesion, as found at operation, without, of course, revealing its true nature. Until these cases of syphilis of the stomach were subjected to x-ray examination and subsequently operated upon, certain roentgenologic changes in the appearance of the stomach were thought to be characteristic of gastric cancer or linitis plastica, which is intimately related to scirrhus cancer.

According to the seat of the lesion in either the vertical or transverse stomach, two types of cancer, and now of syphilis, are recognized. The one type, in the vertical stomach, shows the characteristic changes due to segmentation, and in the transverse stomach, the changes due to obstruction. These changes I have explained at length in previous publications, and they are readily understood by accepting Forrsell's anatomic studies. In my case, the second or

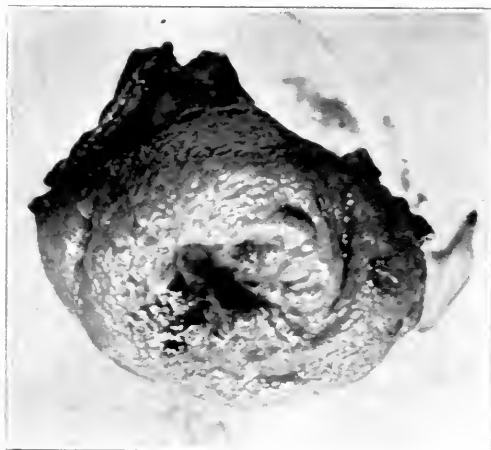


Fig. 1.—Gastric aspect of the mucosa with multiple ulcers.

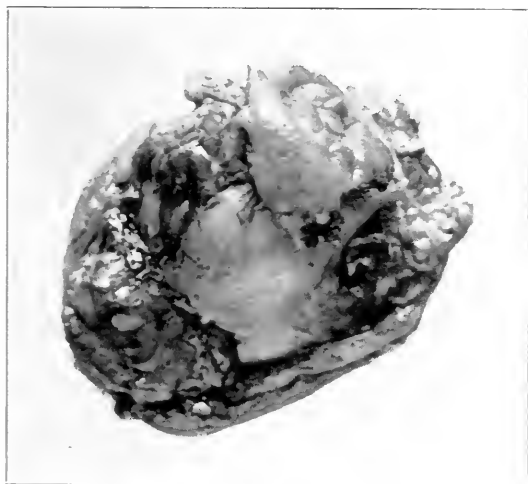


Fig. 2.—Duodenal aspect of the mucosa.





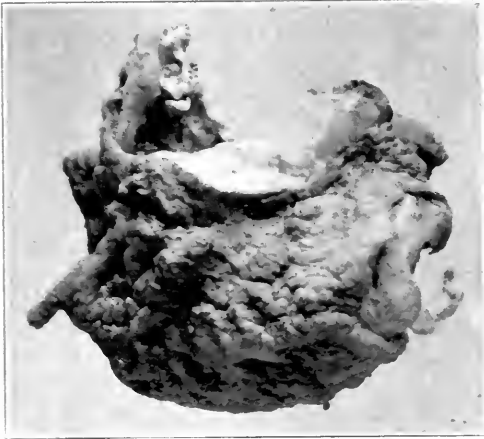


Fig. 3.—Section of the resected portion.



Fig. 4.—Section through the denuded mucosa, the thickened submucosa with multiple gummata, and the thickened circular and longitudinal muscularis.



Fig. 5.—Roentgenogram of the stomach at rest with the patient prone.



obstructive changes predominate, with a typical distal canalization or plug into the tumor mass, and the proximal dilatation and enormous peristalsis seen fluoroscopically in obstruction of long standing.

Besides these x-ray findings, the other data are characteristic, but not new.

The history is that of a bookbinder, single, age 51, chancre at 25, no treatment, gonorrhea at 30, typhoid at 35.

Often hoarseness, "eczema" on hands which patient traced to his profession.

Stomach symptoms since March, 1916, sharp pains an hour after meals lasting an hour or two. At first relief from treatment. In June, 1916, the pain became constant, and increased after meals. Treatment continued, lavage and laxatives until September, 1916. Was then fluoroscoped in Chicago, and thereafter treated for gastric ulcer. In December, 1916, after six months' treatment, the physician at last opened him up at a Chicago hospital and found what he thought was a slow-growing flat cancer. Patient had already lost 35 pounds.

On February 21, 1917, patient is seen by Dr. Carl Beck. He complains now of intermittent pain in the stomach, but only after dinner and supper, not after breakfast. Onset one hour after the meal, lasting two hours and coming on again the latter part of the night. Patient says he is now gaining in weight.

Physical examination reveals the abdomen distended, but containing no free fluid. Midway between umbilicus and right costal margin, on deep inspiration, a nodular tumor is palpable. No visible peristalsis. Spasmodic contractions and relaxations of the pyloric sphincter palpable.

Wassermann taken shows one plus.

Laryngologic examination explains the hoarseness as being due to a total paralysis of the left vocal cord.

Operation Feb. 28, 1917. Median incision beginning below the ensiform. On opening peritoneal cavity omentum was found to be adherent to abdominal wall scar, seat of previous operation. On examination of the stomach, the pylorus and lesser curvature, about the lower one-third, was found to be pathologic. It was decided that a resection of the affected part should be done. Omentum and mesentery of greater and lesser curvatures adjoining the pathologic area were clamped, excised, and ligated. Stomach is grasped with a crusher just above and below the affected area. The area was excised. Two rows of through-and-through sutures were used to close the incisions in the bowel, all bleeding points being stopped. A third row of Lembert sutures was used to invert the stomach. Tissue, especially at the lesser curvature, was very friable, ligature material tearing through frequently. Following the closure of both ends of the bowel in this manner, an anterior long loop gastroenterostomy was performed, no clamps being used, and three rows of sutures, two of chromic gut and one of silk. Several anchor sutures were used to keep bowel from angulating at site of anastomosis. On examination of the bowel, in many places the small intestine showed areas which might simulate a luetic condition (typhoid in history). A grayish adhesion noticeable between coils of the bowel. A drain was left in the region of the pylorus, and the abdomen closed in the customary manner.

## SOME DIFFERENTIAL POINTS BETWEEN CANCER AND SYPHILIS OF THE STOMACH

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THIS is not intended as a disquisition on cancer or syphilis of the stomach, nor is it a textbook study of either. I will endeavor to briefly record certain impressions that have seemed helpful in differentiating these two maladies in which the prognosis is so variant—impressions that have on several occasions enabled me to avoid embarrassing diagnostic pitfalls.

The human picture of advanced gastric cancer, with its concomitant disturbances is rather characteristic. The cachexia, the anorexia, the marked loss of weight, the general appearance of "goneness"—all these are familiar to the physician of experience. When a test meal from the stomach shows little or no free hydrochloric acid, the presence of lactic acid, and perhaps the Boas-Oppler bacilli, another diagnostic link is forged. If, in addition, the roentgen examination portrays a deformed stomach, with serrated margins of the shadow; and when all these malign manifestations appear in an individual past middle life, who gives a history of either long-continued digestive distress, or a recent digestive "debacle," accompanied by the rapid onset of all these symptoms, a mere tyro could make the gloomy diagnosis.

On the other hand, there come to us sufferers who have not reached middle age, but who exhibit many indications, both objective and subjective, of gastric cancer.

In some a history of syphilis may be elicited; in others, both the character and station in life would absolutely negative such a suspicion. Here is where a Wassermann should be a deciding factor in clarifying the fog, but unfortunately it is in many instances a "broken reed." At the risk of being dubbed an iconoclast, I wish to



Fig. 1.—Normal stomach shadow of short, compact individual. All portions well filled out.



Fig. 2.—Early, operable cancer of pylorus. Note ragged and serrated shadow.





Fig. 3.—Syphilis of stomach in individual twenty-two years of age. Now clinically well.



Fig. 4.—Cancer of body of stomach. Note "worm-eaten" appearance of lesion.





record my skepticism concerning the present-day Wassermann. Four plus reports have been given me, when neither past history nor subsequent events substantiated the diagnosis of lues; while negative Wassermans have been "turned in" for patients who were undoubtedly syphilitic. Until some fixed technical standard is reached, or certain scientific requirements are demanded of those who perform these delicate tests, the Wassermann will continue to be in a large number of instances, instead of a light in the darkness, a "delusion and a snare."

Two quite important considerations are the age and general appearance of the patient. Gastric carcinoma is seldom encountered under the age of forty or fifty-five, and more often after the latter age. It is easy to believe that some of the reported cases of cancer in young persons, where inoperable neoplasms were found in the abdomen, were really syphilis. Then, too, these sufferers, though the gummatous growths invading the stomach have greatly curtailed its motor and digestive capacity, thereby causing weakness and emaciation, do not generally "look the part" of cancer. The cachexia may be, and often is, entirely absent.

The clinical and microscopic findings in a syphilitic stomach are not very helpful from a differential standpoint. The oxyntic or acid-bearing zone is in the middle portion of this viscus, so that any form of hyperplasia there will bring about an achylia. Stagnation of any sort in the stomach may promote the presence of either lactic acid or the Boas-Oppler bacilli, which in themselves are not at all pathognomonic of cancer. Furthermore, a cancer or gumma, which does not invade the middle zone, or obstruct the pyloric outlet, may play havoc with the patient, while the chemic processes of the stomach remain comparatively normal.

The roentgen findings, when thoughtfully and intelligently interpreted, in a large percentage of cases, cast some real diagnostic light upon this murky subject. In the presence of malignancy, except in the cirrhotic or "leather bottle" stomach found only in those of advanced years, the roentgenogram delineates a distorted organ with edges either *serrated*, or, where it is not filled out, exhibiting a ragged or "moth-eaten" appearance. In gummatous infiltration, the stomach shadow appears to be either almost *blotted out*, or blurred by more rounded masses. I am prepared to go on record that I have never seen a true

sypilitic stomach show either *serrated* edges in the shadow, or the appearance of either moth-eaten fabric or worm-eaten wood, as have been noted in true cancer cases. This will be illustrated in the accompanying cuts.

Where the element of time is not urgently demanding a quick answer, active antiluetic therapy will, in most instances, afford prompt amelioration of all distressing symptoms; or, if the condition is malignant, will make bad matters worse so quickly that a decision will be simply *thrust* on the medical attendant.

There might also be mentioned the possible contingency of both an old degenerating ulcer of the stomach, plus a gummatous invasion. Such as this could only be judged on its merits, and treated perhaps empirically, while waiting for the "clouds to roll away."

Let it be emphasized in conclusion that the stain of syphilis is widespread, that it abides in the palaces of the mighty, as well as the abodes of the lowly; that the most devout churchman may unwittingly harbor this ubiquitous taint, while the beautiful young maiden, in her innocence and purity, may, nevertheless, entertain this consuming guest, that will

"—Like a worm i' the bud,  
Feed on her damask cheek."

So, in all organic changes of the stomach, before pronouncing the sorrowful diagnosis of cancer, let every effort be made to eliminate any doubt as to the existence of this ancient but omnipresent enemy to mankind.



Fig. 5.—Syphilis of stomach in woman of twenty-eight. After energetic antiluetic treatment, she is now clinically well.

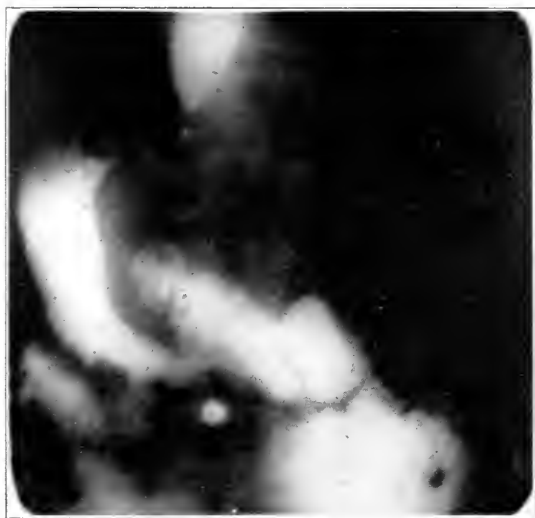


Fig. 6.—Advanced, inoperable cancer of stomach. Note plain serrations of lower part of stomach.



## REPORT OF A CASE, WITH DISCUSSION

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### ANAMNESIS

Mrs. —, white, age twenty-five, married, place of examination, office; date, June 22, 1917.

*Chief Complaint.*—Pain in the epigastrium, of about 18 months' duration.

*Present Illness.*—Last August had an attack of illness, characterized by pain in the epigastrium, vomiting, hematemesis and some fever. The attack lasted four or five days and was followed by soreness in the abdomen. She does not know how much blood she vomited, but says it was a considerable amount—at least a pint. After two or three months she had a similar attack, but did not vomit blood. Since that time she has had frequent attacks. Sometimes she has vomited blood, but has passed more blood, which is always dark, through the bowels. The attacks are also at times accompanied by diarrhea and sometimes by fainting spells. She frequently feels well when she first arises in the morning, but soon the bowels begin "to run off" and she feels very bad. She does not think that the attacks are produced by indiscretions in diet, nor is she certain that the pains, which have been more or less constant, gnawing, sometimes severe, have any regular occurrence after meals. The pains are not relieved by taking food, nor by alkalies. She is also uncertain with reference to the fever. She has lost about 33 pounds in weight since the present trouble began.

*Epitome of Symptoms.*—Epigastric pain of varying degrees of severity, however, never severe enough to require an opiate, without reference to meals; vomiting, sometimes marked; hematemesis, melena, matutinal diarrhea, general abdominal tenderness, loss of weight.

*Previous History.*—She had none of the diseases of childhood; her bodily functions in early life were good and she had no serious illness until after her first marriage. Her habits have been good; her education fair, and experience is limited.

*Marital History.*—She has been twice married. During the period of her first marriage she had three miscarriages, the first being near full term, the other two at three and four months. There was evidence of septic infection at the first and third. Two years ago she had an operation for "flooding" and the appendix, right tube and ovary were removed at that time. She has had two miscarriages, the last six weeks ago, since her second marriage, two years ago. Her first husband was known to have had syphilis.

### STATUS PRESENS

*General Points.*—There is no abnormality in her gait; she is undernourished—her height 5 ft., 2 in., and weight 90 pounds; the musculature is flabby; she is in-

telligent, giving a very good account of her history; the skin and mucous membranes are pale; temperature, 98° F.; the cervical and epitrochlear lymph nodes are distinctly palpable; there is no abnormality of bones or joints; the radial pulses are equal, regular and 84 per minute; the systolic blood pressure is 100 mm. and the diastolic 65 mm. (auscultatory).

*Regional Examination.*—The head, neck, and thorax are normal. Krönig's isthmus is narrow on both sides; at both apices, the expiratory sounds are prolonged, the whispered voice sounds are somewhat increased, both more marked on the right. There are no rales at either apex after coughing. Fluoroscopic examination shows slightly increased density at both apices, possibly more marked at the left. The maximum intensity of cardiac impulse is in the fifth interspace, 3¾ cm. from the midsternal line. The area of cardiac dullness is not increased. The orthodiagram gives: Mr. 3.8 cm., Ml. 8 cm., Tr. 11.8 cm., Lm. 13 cm. The heart sounds are clear and no murmurs are present.

The contour of the abdomen is normal. The smooth liver edge is palpable on deep inspiration. The spleen is not palpable. No masses can be felt here. The skin of the abdominal wall is not hyperalgesic. There is slight general abdominal tenderness on firm pressure and a special point of tenderness an inch above and an inch to the right of the umbilicus. There are no tender points in the back.

*Pelvic Examination* (McGehee) shows absence of the right tube and ovary; the uterus not freely movable, and the left tube and ovary enlarged and tender.

The pupils are regular, equal, and react to light and distance; von Graefe's, Dalrymple's, Stellwag's, and Moebius' signs are absent; Rosenbach's sign is positive. There are no disturbances of sensation or motion; the superficial and deep reflexes are normal.

#### LABORATORY FINDINGS (COLBERT)

*Blood.*—Leucocytes, 6,600; polymorphonuclear, 66%; small lymphocytes, 31%; large mononuclears, 29%; eosinophiles, 1% (number counted 250); erythrocytes 3,800,000; hemoglobin percentage 55% (Sahli); C. I. .7 plus; slight anisocytosis; Wassermann (Noguchi) reaction, positive four plus.

*Urine.*—Single specimen, amber; specific gravity, 1.008; acid; no albumin; no sugar; no casts; no red blood cells; a few pus cells and motile bacilli.

*Sputum.*—Obtained 6/23, 7/1 and 7/6, did not show tubercle bacilli.

*The temperature*, taken daily, at 8 A.M.; 12 M.; 4 P.M.; 8 P.M.; from June 24 to July 1, did not show any variation from the normal daily temperature curve.

After a Dock test breakfast, on a fasting stomach, the fractional examination of the stomach contents is shown in Fig. 1.

Stomach low, digestion delayed, occult blood (Benzidin test) in 1 hr. and 2 hr. specimens positive.

*X-ray Examination.*—(Cullings) 6/25/17. Preparation, no breakfast. Character of opaque meal 4 oz. barium; time of meal, 11 A.M.; time of first observation 11:05 A.M.; time of first plate 11:10 A.M.; position of stomach, low; shape, normal; deformities slight at cap; character of peristalsis, increased; filling defects, absent; incisuræ, absent; Bishop's cap, slight irregularity; time of further observation 5:30 P.M., first and second portion of duodenum dilated, about ¼ of opaque meal in stomach.

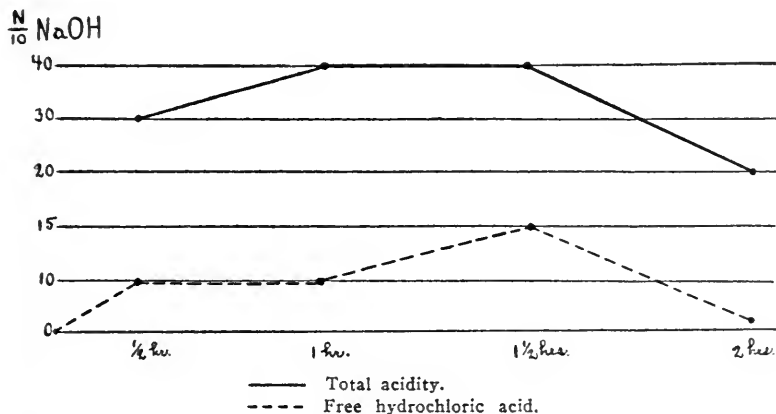
A probable diagnosis of gastrointestinal syphilis was given and active anti-syphilitic treatment—salvarsan intravenously and mercury salicylate intramuscularly—advised.

#### CALTUMNESIS

Salvarsan was declined on account of financial reasons, but she was given 12 doses of mercury salicylate (1 gr. each) at intervals of one week, by her home physician, who writes that this treatment was followed by marked general improvement and subsidence of gastrointestinal symptoms.

#### DISCUSSION

A discussion of this case will necessitate a consideration of gastrointestinal syphilis—admittedly a rare condition. "Manifestations



of syphilitic infection, though comparatively common at the two ends of the alimentary canal, are very rarely recognized in the intervening portions." (Dreschfield.)

In a careful review of the literature of gastric syphilis one encounters difficulty in determining accurately the frequency of this condition. This is due to the different criteria upon which the determination is based; some of these criteria being doubtful, others questionable. The earlier literature deals with the anatomic diagnosis from postmortem material, and all of these cases are, of course, well authenticated.

One is struck with the infrequency of these cases. A few single cases, reported by different observers (Andral, Cornil and Ranvier, Klebs, Weichselbaum and possibly a few others) appear in this

early period. Chiari, by a pathologic study of 243 autopsies on syphilitic cases, could find among them only 2 cases of gastric syphilis, and regarded only 8 of those which had been reported previously as authentic.

Flexner, in 1898, in reporting a case of syphilitic ulcer of the stomach could only find fourteen trustworthy cases in the literature up to that time. "Aristoff, on the other hand, maintains that careful histologic examination of the stomachs of luetic subjects frequently reveals syphilitic changes in the form of miliary gummata and diffuse syphilitic inflammation." (Kohn.) Sometimes, however, the pathologist is in doubt as to the anatomic diagnosis. (Downes, Wm. A., and Le Wald, Leon T.).

The frequency increases greatly when determined on a clinical basis (Einhorn, Kohn, Hemmeter, Seigheim, Mathieu, Fenwick, Meyer, Morgan, Clark, Smithies, McNeil, Portis, Eusterman and others). The basis of clinical determination has varied greatly; e. g., the occurrence of gastric symptoms in a known syphilitic; a history of syphilis, stomach symptoms, which improve or disappear under specific treatment; dyspepsia, gastric pathology and a positive Wassermann. These are all questionable criteria for a positive diagnosis. Gastric symptoms may occur in syphilitics as the result of general inanition and anemia (Kohn); as the result of reflex disturbances from syphilitic lesions of other organs (McNeil), and there is "a group of cases in which a tumor, believed to be in the stomach, is really due to a gumma of the left lobe of the liver, adherent to the anterior wall of the stomach, closely simulating carcinoma of the stomach" (Osler and Gibson). The gastric symptoms may themselves be dependent upon the mercury and potassium iodide and disappear with the general improvement and discontinuance of the treatment.

No one will doubt the very great help which the Wassermann test has afforded us in determining the presence of active syphilis. However, possibly too many mistakes in diagnosis are made by attributing various diseased conditions to syphilis, because the patient's blood happens to give a positive Wassermann reaction. A gastric ulcer, a pyloric stenosis or a tumor of the stomach, which has no etiologic relationship to syphilis, may occur in a patient with active syphilis, as shown by the positive Wassermann.



In the clinic in which I work, a large proportion of the pneumonias give a positive Wassermann, indeed in the last two years among more than two thousand admissions for various conditions, more than 35 per cent gave a positive Wassermann reaction. Still we do not attribute the pneumonias and the various conditions in patients giving a positive Wassermann to syphilis. Judging from the literature, there is no clinical syndrome pathognomonic of gastric lues, nor are there any laboratory or x-ray findings which alone are characteristic of the condition. It is well to remember the old maxim, "When in doubt, suspect syphilis."

The symptoms of a chronic gastritis, with a history of syphilis or positive Wassermann reaction, intractable to ordinary treatment, and yielding to specific treatment, would seem to be sufficient grounds for a probability diagnosis of a diffuse syphilitic gastritis. So also ulcer symptoms, with marked loss of weight, a diminished or absent free hydrochloric acid in the stomach contents, the x-ray findings of gastric pathology, an hourglass contraction, possibly with absence of a niche, accessory pocket, or typical incisura; a positive Wassermann and favorable response to specific therapy, justifies a probability diagnosis of syphilitic ulcer of the stomach.

Gastric symptoms of long duration, a positive Wassermann, subacidity or anacidity, marked filling defects, lessened motility, absence of peristalsis, gaping or obstructed pylorus, with or without palpable tumor, and loss of weight, which respond favorably to antisiphilitic treatment render hyperplastic syphilis of stomach probable.

It must not be forgotten, however, that syphilis of the stomach is sometimes present in spite of a negative Wassermann. (Einhorn, Eusterman), and sometimes the symptoms of obstruction, due to scarring, may not be relieved by antisiphilitic treatment. The probable diagnosis can only be confirmed by histologic examination of the tissue, removed either at biopsy or autopsy. Syphilis of the intestines, exclusive of lues of the rectum, is even less frequent than gastric syphilis. "The duodenum may be attacked with the stomach. The most frequent region for the small intestine to be affected is in the lower part of the jejunum. The colon alone has been found to be the seat of the disease, but it is in the rectum that

syphilitic affections are common; in the rest of the intestines they are extremely rare." (Osler and Gibson.)

Cases have been reported by Bittner, Hayem and Tissier, Hueter, Gutman, Hömen, Fraenkel, Kohn and Haller (D. A.) and Walker (I. C.). I have seen one case in a distinguished member of our profession. A syphilitic infection was accidentally acquired many years prior to his death. Several years before death the patient suffered from symptoms suggestive of duodenal ulcer and his case was diagnosed as duodenal ulcer by an able gastroenterologist. Finally he had indications of a perforation and at operation three ulcers were found close together in the jejunum—one of them had perforated. The ulcers were annular tending to produce stenosis, with ragged edges and a smooth pale base.

Our case, here reported, shows evidence of past and present syphilis. Husband luetic, repeated miscarriages, without apparent cause, adenopathy and a positive Wassermann-Noguchi reaction—loss of weight and subacidity. The x-ray findings might be interpreted as an obstruction due either to perigastric adhesions or an ulcer in the lower part of the duodenum. The hematenesis and melena make ulcer more probable. The favorable response to treatment renders it probable that the lesion was of a syphilitic nature.

## SYPHILIS OF THE LUNGS

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THE waging of war nowadays, just as surely as history repeats itself, will cause a great increase in the prevalence of all venereal diseases. In addition, the increasing belief and indulgence in so-called "free love" will undoubtedly help to cause many medical burdens and much suffering, by spreading the seeds of syphilis. Indeed the daughters of Moab are more than historical characters.

With the increase in the prevalence of social diseases incident to the changed social conditions of the present, the germs of syphilis will probably exert their influence more on the lungs than they have in the past. The pale spirochete nestles and breeds within the tissues of an appalling number of people. However, the lungs are one of the rarer locations of luetic changes. Yet the occurrence of pulmonary pathology of syphilitic origin is not so rare as some suppose. The apparent rarity is due partly to the fact that the condition resembles tuberculosis so much, in some cases, that the latter condition receives the credit for the symptoms of the former disease.

The classification of syphilis of the lungs usually is dependent upon the prenatal or postnatal beginning of the luetic process. *Inherited syphilis* is of two types—circumscribed and diffuse. According to Fowler, *acquired syphilis* manifests itself in one of the following forms: (1) gumma, (2) bronchopneumonia, (3) fibroid induration or chronic interstitial pneumonia, or (4) a progressive destruction of the lung—the so-called syphilitic phthisis.

*Inherited gummata* of the lungs are rare and differ in no way from the acquired gummata.

*Inherited syphilitic pneumonia*, or the diffuse type, is known either as "white pneumonia" or "interstitial pneumonia."

White pneumonia is a diffuse change occurring in the lungs of stillborn children or in babies who live but a few hours. In this,

part or all of a lobe is usually affected, although an entire lung or even both lungs may be affected. The surface of the lung, which is enlarged, often shows the impressions of the ribs. In addition to the enlargement, the lung is white or greyish-white in color, heavy, dry, and, in the case of stillborn babes, is devoid of air and blood in the affected area. Thickening of the alveolar walls occurs. The alveoli are enlarged and filled with masses of cells which usually are degenerating. These degenerating cells are often present in the small bronchi. In the cases which survive a few hours, the blood supply to the affected part is much less than normal. In cases of white pneumonia, characteristic signs of inherited syphilis are nearly always present, and the baby is frequently born before full term.

Interstitial pneumonia usually occurs as part of a general syphilitic process, the victims of which live but a short while. The chief pathologic features of this form are a small-celled infiltration of the interalveolar connective tissue; a marked increase of the interlobular connective tissue; an increase of connective tissue around the vessels and bronchi; a thickening of the tunica intima of the arterioles; and, in some cases, the enclosing of a network of dilated and tortuous capillaries, by strands of interalveolar connective tissue.

In the acquired type of pulmonary syphilis, the *gummata* resemble gummata in other situations. Ranging in size from that of a small pea to that of a hen's egg, they may occur in all parts of the lung but usually select the substance of the lung in the vicinity of the hilus. These gummata may be single or multiple; they may caseate, but usually tend toward the formation of cicatricial tissue, which scar tissue causes a shrinkage of the surrounding lung substance as well as a dimpling of the lung surface and the adherent pleura.

*Syphilitic bronchopneumonia* is, in the opinion of some observers, a doubtful condition. In the case reported by Delepine and Sisley, an enormous gumma of the right lobe of the liver, measuring  $5\frac{1}{2}$  by  $4\frac{1}{2}$  inches, and adherent to the diaphragm, pushed up and extended through the diaphragm, and involved the lower lobe of the lung. In this case, in addition to sclerotic induration, there were patches of lung tissue resembling catarrhal pneumonia and there were patches of caseous pneumonia. This condition resulted from a direct extension and surely was not an ordinary pneumonia.

*Chronic interstitial pneumonia*, or fibroid induration, is a process in which long strands of connective tissue, which often radiate from the hilus of the lung and which more or less surround the bronchi and vessels, and in which patches of sclerosis or areas of diffuse fibrous changes affect a lobe or even an entire lung.

*Syphilitic phthisis* is undoubtedly rare. In order to be certain of the existence of this form of lues, Fowler, who has probably done more work in the investigation of pulmonary syphilis than any other man, lays down the following postulates: (1) the case must be complete; that is, the symptoms observed during life must be considered in connection with the lesions discovered on postmortem examination; (2) the evidence of syphilitic infection must be undoubted; (3) repeated examinations of the sputum must have been made, and tubercle bacilli invariably absent, and the absence of tubercle from the lungs (as the cause of the lesions) must be proved by postmortem examination; and (4) syphilitic lesions, about the nature of which there can be no doubt, must be found in other organs. From the foregoing, it is evident that positive diagnoses of this progressive syphilitic wasting of the pulmonary tissues will be few and far between.

In many cases of recurring bronchitis, emphysema, and asthma in young men and women, Lerrede has reported obtaining positive responses to serologic and clinical tests for syphilis. All of these cases reported by Lerrede had been inclined, since childhood, to dyspnea on muscular exertion; and several were troubled with emphysema; and some had real asthmatic paroxysms; and all had certain or probable hereditary lues.

It seems not improbable that syphilis and tuberculosis of the lungs coexist more frequently than some of us suspect. The fact that some of us never consider the possibility of such an occurrence makes the overlooking of the luetic infection extremely easy. Fowler calls attention to the chief points of difference between the pulmonary lesions of syphilis and tuberculosis in the following words:

"1. Tuberculosis usually affects the apex of the lung, and, subsequently, the apex of the lower lobe, and tends to progress along a certain route. The primary lesion of syphilis is often about the root and central part of the lung; the disease follows no definite line of march, and gummata may be found in any position.

"2. Both gummata and tubercles may undergo either necrosis and caseation or fibrous transformation; but with caseous tubercle, the tendency towards softening and cavity formation is the rule, whereas a caseous gumma very rarely breaks down.

"3. The progressive destruction of the lung by a process of disintegration leading to a gradual increase in the size of a cavity, a change so often observed in tuberculous disease, is rarely, if ever, present in syphilis, except as a secondary result of stenosis of one of the main bronchi.

"4. In nearly all advanced cases of destruction of the lung occurring in the subjects of syphilis, stenosis, either of the trachea or of one of the main bronchi, is present; whereas this lesion is very rare indeed in tuberculosis.

"5. The cavities found in cases of pulmonary syphilis are usually bronchiectatic, but not invariably so; whereas in tuberculosis, they are commonly due to progressive destruction of the lung, but may be bronchiectatic.

"6. The tendency to the formation of pulmonary aneurysms, which is so marked a feature in tuberculosis, is rarely observed in pulmonary syphilis.

"7. Pulmonary lesions in tuberculosis are very common, whereas, in syphilis, they are extremely rare."

The *symptoms* of syphilis of the lungs are not particularly distinctive. Probably the earliest and most frequent symptom is *coughing*,—which coughing is due to either irritation of the bronchi or trachea or to changes within the lung. The coughing produces usually much *offensive sputum*, which in cases not complicated by tuberculosis, does not contain tubercle bacilli. *Hemoptysis* is not infrequent; at times the blood is sufficient only to tinge the sputum, but at other times is more plentiful. *Dyspnea*, which is due more frequently to stenosis of the trachea or one of the larger bronchi than to changes within the lungs, is not uncommon. *Fever*, which is usually of the tuberculous type, occurs practically always in the cases in which there is extensive involvement. Pain, emaciation, and night-sweats may occur.

The *physical signs* are, like the symptoms, not characteristic. These signs are dependent on the character of the lesion,—consolidation and cavity formation producing their usual signs.

The Wassermann test, or one of its modifications, is almost invari-

ably strongly positive. The cell count and globulin content of the spinal fluid is characteristic of syphilitic infection. Mayer and Gourdy assert that, in all cases of syphilis—irrespective of the part most involved—a lymphocytosis is a constant sign of syphilitic infection; that this lymphocytosis appears prior to the Wassermann reaction; and that the lymphocytosis persists throughout life, as an indelible sign of syphilis.

The *prognosis* of the ordinary cases of lues of the lungs is good. The average patient suffering with this manifestation of infection by the spirochete pallida will do well under intelligent treatment. In the form known as syphilitic phthisis, the chances of recovery are few. In the congenital forms, as was stated previously, death occurs prior to parturition or soon after birth.

The *diagnosis* becomes a task of distinguishing lues from tuberculosis. It is quite evident that, when these two processes coexist, the diagnosis of both is extremely difficult. Wassermann tests of either the blood or spinal fluid are invaluable. Repeated examinations of the sputum are necessary. A differential white cell count, according to the above-mentioned Mayer and Gourdy, would be helpful.

The *treatment* of the pulmonary manifestations of lues differs in no respect from that of syphilis elsewhere. The cause of all luetic lesions is the pale spirochete, and the therapeutic measures which will affect the activity of this organism in other parts of the human body will have a similar effect upon that germ in the lungs. At the present time, the chief remedies are mercury, potassium iodide, and the arsenical compounds.

Mercury is administered orally, intravenously, intramuscularly, intraspinally, and by inunction. The protoiodide and the bichloride seemed to be used more than any other forms of mercury. The thirty per cent calomel ointment, made up in cold cream, is an excellent method of administering the drug, because it is cleanly and quickly absorbed by the skin. Using a combination of colloidal mercury and colloidal sulphur (in which combination the sulphur is said to increase the tolerance for mercury), Loeper and his coworkers have secured very favorable results.

Potassium iodide is very valuable in the treatment of the tertiary lesions of syphilis,—and the pulmonary form is one of these.

Of the arsenical compounds, salvarsan, diarsenol, and arsenobenzol have given the most satisfactory results. These preparations are

best given, in cases of pulmonary syphilis, intravenously in doses of 0.5 gram or 0.6 gram once a week for ten or twelve weeks successively. Schamberg, Kolmer, and Raiziss have given arsenobenzol orally in the following combination: arsenobenzol gm. 0.03 or gr.  $\frac{1}{2}$ ; sodium hydrosulphite gm. 0.015 or gr.  $\frac{1}{4}$ ; and bismuth subgallate gm. 0.12 or gr. ii,—which is administered in gelatin-coated capsules which have been treated with formaldehyde. One such capsule, followed by water, is taken after each meal.

The usual practice is to follow a course of treatment with one of these arsenical preparations by a course of mercuric medication. However, Bory has obtained excellent results by a reverse order of treatment. Anyway, the courses of mercury and of the preparations of arsenic should be alternated, with short periods of rest between each succeeding course. The subsidence of symptoms and the clearing-up of physical signs do not mean a cure of syphilis. The treatment is of necessity long and trying. It is most inadvisable to consider any one free of the pale spirochete and its toxins until the spinal fluid fails to give a positive reaction to the Wassermann test for several years after the last administration of antiluetic measures.

In cases in which syphilis and tuberculosis coexist, the treatment first should be toward the more extensive lesion.

Syphilis of the lungs results from an untreated or insufficiently-treated case of ordinary lues, and, therefore, should never occur. And it would probably never occur if there were some means of detecting each case in the primary stage and of compelling such persons to take proper and sufficient treatment.

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## LEUCOPLAKIA OF THE TONGUE

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THE following instance of leucoplakia is interesting for several reasons: Because of its occurrence in a young man, because of its association with syphilis, and because it almost entirely cleared up under the use of radium and antisiphilis treatment.

A slightly built, rather delicate man of twenty-two years of age, called on me May 22, 1917, on account of a white patch on the left side of the tongue.

The patch was thick, leathery, and was as dead white as plaster. It was sharply circumscribed, and about 1x2 cm. in area. It gave rise to only mental discomfort. The patient said that at the age of fourteen a small "spot" appeared on the left side of the tongue below the edge. At first the spot would come and go, but from sixteen years of age it had remained permanently. At fourteen years he had had a sore on the left thigh just below the buttock, and from then on he said he had suffered from a persistent catarrh of the nose.

In the course of the examination the patient showed me a scar on the left side of the penis, just behind the sulcus, which he said arose from a venereal sore acquired at sixteen years of age.

There was no doubt the patient dated his ill health from fourteen years of age, but I am inclined to date his syphilis from sixteen. I would therefore regard the sore on the back of the thigh as a furuncle, and would ascribe the scar on the penis to his initial luetic lesion. He admitted being at that time exposed to such a contagion.

The patient also showed me a scar on the ulnar side of the left wrist, due to a purulent infection, which occurred one year previously and which he thought arose from an injury. It was impossible to tell if this was luetic.

As regards his general health, the patient was of frail build, no friend of exercise, addicted to sugar, somewhat constipated, had a palpable descending colon, and from fourteen years of age on, as previously mentioned, had a persistent catarrh of the nose. In

May of the preceding year (1916) he had a purulent discharge from the eyes, with redness of the lids. Redness of the edges of the lids and sensitiveness to wind still persisted.

He had a wet mouth which was probably due to mercury, which he had been taking, although the gums were not inflamed.

He said he had never smoked, or used tobacco in any way. This is important, considering the usually, and undoubtedly justly, accepted view that one of the chief causes of leucoplakia is tobacco smoke.

Just previous to consulting me, the patient had received what seemed to me to be a very inadequate antisyphilitic treatment by the mouth. In the previous January he had suffered from a severe cough from which he had not entirely recovered. Because of the cough, and because of the mild salivation, and also from a desire to get a Wassermann test uninfluenced by mercury, no antiluetic treatment was instituted at this time.

The leucoplakia was treated with radium. A dime-sized plaque containing 24.23 mg. of radium element, and screened with A1. 0.05, cotton and rubber, was applied for ten minutes on May 22, 1917, and reapplied in ten days. In two days after this last application a rather severe, quite painful reaction was obtained. In two weeks the hyperkeratosis had entirely disappeared, leaving what appeared to be a slight scar. There was now also on both sides of the tongue, but especially on the right side, an opalescent haze such as one associates with syphilis, although not definitely characteristic of it.

On June 28, his blood was found Wassermann positive, and on July 27, he received a salvarsan (0.4) infusion intravenously, and four days afterwards he began a course of intramuscular injections of grey oil.

Five weeks after the infusion of salvarsan it was noted that there was only a faint opalescent haze, irregular in shape, and with sharp boundaries, on the left side of the tongue where the leucoplakia had been, and that this haze seemed to be growing fainter.

In all, the patient received two infusions of salvarsan, one of 0.40 and one of 0.60, and twelve injections of 0.07 grey oil. This treatment extended over a period of ninety-five days. The tongue never entirely cleared up; there always remained the opalescent haze and decided local sensitiveness. This residual sensitiveness was inter-

esting, as usually in such cases treated with radium, the sensitiveness disappears, and it indicated that there was more present in this situation, in this case, than simply leucoplakia.

#### DIAGNOSIS

The dead white color, the leathery consistency, and the permanency of the patch all indicated it as a leucoplakia. It certainly was not a patch of lichen planus, or a traumatic lesion from rough teeth. A mucous patch would not be so permanent, and it would not be so thick, leathery and plaster white. Of course, the ultimate diagnosis of syphilis is another matter, as there are those who believe that leucoplakia is always a manifestation of syphilis (Landousy, Gougerot).

#### THE PROBABLE SEQUENCE OF EVENTS IN THE CASE OF THE PATIENT UNDER CONSIDERATION

The sequence of events in this man's case seems to have been:

1. An irritable area, possibly herpetic, on a sensitive mucous surface, covered by stratified epithelium, the only kind of epithelial surface on which leucoplakia occurs.
2. A constitution prone to catarrhal inflammations, and sensitized by luetic infection.

The etiology of leucoplakia seems to be by no means a simple affair. Probably the chief cause is syphilis, next comes tobacco smoke, and finally a chronic catarrhal and, therefore, irritable state of the mucous membranes, usually found in connection with chronic fermentative intoxications along the alimentary tract.

When leucoplakia is a manifestation of syphilis, it is not an early symptom of the disease, but a late one. It has been ranked with tabes and the other scleroses of the central nervous system as a parasyphilide. In accord with this etiology, leucoplakia is a disease of middle or advanced life, for a man does not usually accumulate such treasures as tertiary syphilis, chronic tobacco traumatism, and advanced intestinal intoxication until middle life or old age.

As regards the future of this case, it, of course, is uncertain. The condition may return, as leucoplakia is notoriously refractory to treatment. Anything that may ameliorate it or may secure a cure

is of the utmost importance, however, as the condition is now recognized as precancerous, especially when occupying its favorite situation upon the tongue. It indeed forms the most interesting connecting link between syphilis and cancer.

Mercury and iodide of potash are only of temporary benefit, and mercurialism is decidedly detrimental. In fact, mercury, especially when given by the mouth, seems, in many instances, to aggravate it. The best active therapy is salvarsan, which sometimes influences it, and x-rays and radium, which influence it to a much more decided extent. Of the two last, radium seems to be by far the more essentially effective, and is much more easily applied.

## SYPHILIS OF THE INNER EAR AND EIGHTH NERVE

(*Conclusion*)

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IN the latter part of the former contribution on this subject\* I enumerated a list of changes found in the inner ear as the result of syphilis. The list includes practically all those changes which have been noted by various investigators who have had opportunity to study the temporal bones of syphilitics from the pathoanatomic viewpoint. The earlier investigators studied the temporal bones macroscopically as gross specimens, while the more recent investigators studied them microscopically from serially cut sections. Unfortunately, some of the earlier investigators, as well as a few of the later ones, recorded the changes as they appeared in the inner ear only and ignored the findings in the nerve. Furthermore, it has been noted by Mayer, Asai and Hofer that where changes occurred in the inner ear, they were found to have been due to the extension of the syphilitic process from the meninges or nerve, via the nerve or blood vessels; besides, they found the pathologic changes in the labyrinth were never so intensive as they were found in the nerve.

In looking over the literature of the subject, I fail to find a single unquestionable case of syphilitic involvement of the inner ear based upon pathoanatomic findings that was not due to extension of the process from either the nerve on the one side or the middle ear on the other. In the cases reported of inner ear syphilis, especially by the early investigators, there is a sufficient element of doubt in practically every instance to make the reports worthless; for instance, the changes in the blood vessels (endo- and periarteritis) noted by Baratoux, have been denied by every investigator since his time, including Panse, who accepts, however, the hemorrhages found by Baratoux as well as in his own case as being due to syphilis. All other investigators have attributed the hemorrhages in the inner ear to suffocation. Many of the changes in the inner ear noted by

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the early investigators are recognized by the more recent ones as due to suffocation, fouling of the specimen or artefacts from other causes. Another serious objection to the acceptance of many of the case reports is the absence of nerve findings. From the textbooks no reliable information can be gathered, for the authors generally credit everything reported without question since so few of them have made pathologic investigations independently.

The cases that have been studied carefully from the pathoanatomic point of view where the inner ear has been invaded from the tympanic side are relatively few and in these there remains a reasonable doubt as to whether the pathologic process was primarily one of syphilis and secondarily one of suppuration from a mixed infection from other organisms, or whether the case was primarily one of suppuration from a pyogenic infection in an individual suffering from a general syphilitic infection and in whom the syphilis had increased the vulnerability of the infected tissues. In any case it is difficult to tell by pathologic as well as clinical examination just how much of the tissue changes is attributable to one or the other of these two factors (syphilis or pyogenic infection).

From our general knowledge of the behavior of syphilitic lesions in other tissues and the behavior of nonsyphilitic lesions in syphilitic patients, both these views are acceptable to varying degrees in different cases, depending largely upon which of the two influences is the weightier. Typical of this class of cases is the one cited by Gruenberg.<sup>37</sup> He cites the case as one of progressive deafness in the course of a fatally ending lues. The diagnosis of lues was established by the history of a primary lesion in a young man about the middle of January, 1907. By the end of February the patient had developed throat manifestations simultaneously with the characteristic secondary skin eruption. He was given antisymphilitic treatment which was followed by improvement. In November, 1907, the patient had a return of throat symptoms, when he again went under treatment with atoxyl, Hg, and KI. In spite of treatment the patient grew progressively worse, and by May, 1908, had multiple ulcerations on the skin and in the throat, the ulcerations involving the hard and soft palate, epiglottis, pharynx, tonsils, nasal septum and the region of the pharyngeal orifice of the eustachian tube. He finally died January, 1909.

Gruenberg made the first otologic examination in June, 1908, when the patient was complaining of marked impairment of hearing and tinnitus aurium that had started six months after the initial infection.

The autopsy revealed ulcerative gummatous processes of the hard and soft palate, tonsils, pharynx, epiglottis and larynx; miliary gumma of the liver and spleen (?); chronic hyperplastic tumor of the spleen; myocarditis, bronchopneumonia, hydrocephalus, etc., et. int.; ependymitis granularis osteome of the pia mater; cachexia luetica.

Macroscopic examination of the temporal bone by Gruenberg revealed the presence of an amber colored exudate completely filling the tympanic cavity and mastoid cells on both sides which Gruenberg confesses was not recognized during life. Both eustachian tubes contained pure pus. The tympanic membranes were intact. In the tympanic cavity was found yellowish-red-colored newly formed connective tissue enveloping more or less the anvil and stirrup. On the promontory there was a mushroom-like growth of connective tissue containing bone.

Microscopically, the exudate was found to be of a serous nature with a few cellular elements (epithelium, leucocytes, erythrocytes). The pus in the tube was separated from the more serouslike exudate in the tympanic cavity by a distinct drop of mucus. Bacteria were not found in the exudate by the Gram staining method. The character of the changes in the middle ear, according to Gruenberg, speaks for a chronic periostitis.

With the naked eye one could recognize readily in the stained sectioned specimen a small pinhead-sized mass of cartilage in the inner ear near the oval window, which was present on both sides. In the bony capsule surrounding this cartilage the marrow spaces were enlarged, due perhaps to pathologic resorption of the bone. The changes in the membranous labyrinth consisted of a poor differentiation of the various cells that go to make up Corti's organ. Diminution in the size of Corti's membrane. Large spaces, lined with delicate connective tissue fibers, were found in the ligamentum spirale (designated hydropic degeneration by Manasse<sup>35</sup>). The ganglion spirale showed pronounced atrophy, more especially about the basal whorl. The ganglion cells were reduced in number and only a few nerve fibers remained. The greater part of Rosenthal's

canal was occupied with connective tissue. The changes were almost identical on the two sides with the exception of the atrophy of Corti's organ, which was more pronounced on the right side. In the vestibule and the semicircular canals no pathologic findings were detected. No changes were noted in the nerve trunks with the exception of those previously noted in Rosenthal's canal.

Gruenberg concluded from his findings that the patient suffered from an extensive tertiary ulceration of the nose, pharynx and larynx, combined with progressive middle ear labyrinthine deafness, the pathoanatomic foundation of which was a bilateral tubal infection leading to an otitis media chronica seropurulenta, which in turn resulted in newly formed connective tissue describable as a periostitis chronica. Furthermore, on the left promontory there was an exostosis formed partly of connective tissue and partly of bone, the bony part having undergone a process of resorption. The exostosis on the promontory as well as the newly formed connective tissue elsewhere in the middle ear could have resulted, according to Gruenberg, from the long continued irritation produced by the chronic catarrhal inflammation of the tympanic cavity.

Concerning the inner ear changes already noted, Gruenberg believes that the cartilage in the inner ear is merely an anomalous formation which has nothing whatever to do with the syphilis, especially so since Manasse had noted a similar formation in about the same region in a case of progressive deafness from other causes. Likewise the atrophy of Corti's organ and the ganglion cells in Rosenthal's canal have been observed by Gruenberg and Manasse in cases of progressive deafness; however, both are inclined to believe that these changes are met with quite commonly in lues.

According to Boenninghaus,<sup>39</sup> middle ear involvement in the course of a secondary lues of the nose and throat is not uncommon, whereas an involvement of the middle ear with tertiary lues is practically unknown.

In short, from the findings in Gruenberg's case and Logan Turner's, cited by Fraser, it can not be definitely settled as to how much of the changes in the middle and internal ear was due to the syphilis and how much to the chronic seropurulent middle ear inflammation. The changes that were found in the internal ear are not especially characteristic of syphilis; it can not be denied, how-



ever, that syphilis played an important part in the pathologic changes that took part in the middle and inner ear of both cases.

Concerning the deafness that appears very late in the course of syphilis, during the so-called parasyphilitic stage, there is practically nothing known of its pathology. The writer is unable to find in the literature any case report with pathologic findings. That one or more of the cranial nerves are predisposed to primary atrophy in the course of paresis and tabes is a well-known fact. The typical primary atrophy of the optic nerve is recognized by the ophthalmologist and syphilologist as a pathognomic sign of tabes in spite of the fact that the Wassermann reaction may be found as often negative as positive. That the otologist has not recognized the same character of changes (primary atrophy) present in the eighth nerve as often or as readily as the ophthalmologist has in the second nerve is due to the fact that the circumstances are less favorable for the otologist. The ophthalmologist has the advantage of being able to study the optic nerve directly with the ophthalmoscope as well as ascertain the function of vision and the visual field, while the otologist has only the function of hearing to guide him. The history and the Wassermann findings are of the same value as an aid to diagnosis in either instance.

In tabes Habermann<sup>40</sup> found almost complete degeneration of the cochlear nerve and partial degeneration of the vestibular nerve. The nerves were replaced with connective tissue. Here and there were found distinct signs of neuritis still present. These changes speak more for secondary atrophy following a primary neuritis than for a primary atrophy of the nerve and should not be mistaken for primary atrophy.

According to Obersteiner,<sup>41</sup> in tabes dorsalis the spinal cord is by no means affected alone, for the disease affects equally well the peripheral nerves (including the cranial) and eventually also their nuclei. He claims that tabes may be described as essentially a degeneration of the posterior roots in their intramedullary course. He denies the claim of Marie<sup>42</sup> that the process begins in the cells of the spinal ganglion but tends rather to the belief that the degeneration is secondary to a syphilitic meningitis.

In Lissauer's zone, which corresponds to that part of the posterior root where it passes through the pia mater and the thin

cortical layer of the cord, the nerve fibers lose their myelin sheath, the absence of which leads to an increased vulnerability at this point, so that a compression of any kind, according to Obersteiner, be it from a meningitic process, from the shrinking of the pia following a syphilitic meningitis, from an overgrowth of glia cells of the cortical layer of the cord or from the arteriosclerotic thickening of the blood vessels, the results would be the same, so far as the tabetic changes found in the cord are concerned.

The same author in discussing paralytic dementia alludes to the two distinctly different views that have been offered to explain the genesis of the cerebral atrophy found in paralytic dementia. The prevailing opinion is that it is a parenchymatous process, a primary destruction of the cortical nerve cells and the medullary nerve fibers, and secondarily a proliferation of the glia cells to make up for this loss. Another view, and the one accepted by Obersteiner, is that the real process is one of diffuse primary sclerosis of the cerebral cortex which leads to atrophy. The sclerosis is caused originally by an inflammatory irritation in the meninges which in turn expressed itself in the form of a periencephalitis chronica. The resulting multiplication of glia cells produces the sclerosis. The increased multiplication of the glia cells with their numerous processes requires more and more room. They surround and squeeze to death the nervous tissue elements, resulting finally in atrophy. Thus Obersteiner believes, and his conclusions are founded upon the careful study of a large amount of material in the neuropathological laboratories of Vienna, that parasymphilitic affections of the central nervous system (tabes and paresis) are the sequela of a previously existing syphilitic meningitis of a mild degree, or as he expresses, "Entzuendlichen Reizzustand" (inflammatory irritation) of the meninges, which subsequently contracts, causing sclerosis and atrophy of the intramedullary portion of the posterior root in the case of tabes and with hyperplasia of the glial tissue, causing cerebral atrophy in the case of paralytic dementia.

From our present knowledge based upon clinical evidences and Obersteiner's studies of the pathology of tabes and paresis, we may accept (a) primary atrophy of the eighth as well as the second nerve as an accompanying manifestation of parasymphilis; (b) primary atrophy is produced by a preexisting *low grade* syphilitic meningitis;

(c) eventually the pia mater contracts and squeezes the life out of the nerve. On the other hand, in those cases where the syphilitic meningitis is more pronounced, the inflammation spreads to and involves the nerve, so that the clinical evidence of neuritis manifests itself simultaneously with or shortly following the meningitis. Under suitable treatment both the meningitis and the neuritis may subside with manifest improvement of function. At a later period the connective tissue elements in the nerve may contract and produce secondary atrophy, as in the case reported by Habermann, in contradistinction to the primary atrophy about which I am speaking.

The researches of Knick and Zaloziecki,<sup>43</sup> Mayer, Asai, Hofer and many others show that in general syphilis, even in its earlier stages, there is quite often a meningitis, mild though it may be. Next, we know that connective tissue once involved in a syphilitic inflammation, even to a mild degree, is more prone to contract than connective tissue inflamed from other causes. Finally, Obersteiner and other neuropathologists have shown us that parasyphilis affecting the central nervous system causes contraction of the connective tissue elements of the pia mater, so that we may consider parasyphilitic involvement of the central nervous system as the aftermath of a low grade meningitis that was present during the active stage of a general syphilitic infection.

A study of genuine or primary gray atrophy of the eighth nerve from the pathoanatomic viewpoint has hardly been attempted.

#### DIAGNOSIS

As introductory to my remarks on the diagnosis, let it be known to those outside the field of otology, that otologists the world over accept certain clinical tests as positive evidence of involvement of the perceiving apparatus, in contradistinction to other equally certain tests, as positive evidence of disease of the conducting apparatus. By the perceiving apparatus is understood the inner ear and eighth nerve.

With one exception the findings from the several tests, typical of disease of the perceiving apparatus, are identical whether the affection is limited to the inner ear or to the eighth nerve or involves both the inner ear and the eighth nerve. The exception referred to is the galvanic test, about which more will be said later.

The negative history of syphilitic infection as well as a negative Wassermann made from the blood or spinal fluid, like negative findings generally, proves nothing. A positive finding, on the other hand, is vastly more dependable; so that in the presence of a negative history of syphilis and a negative Wassermann test, we are dependent largely upon the local findings supported by well recognized evidences of syphilis in other parts of the body; for instance, in the case of suspected congenital syphilis, by the appearance of the teeth and the eyes; in very late lues of the acquired form by the anesthetics, loss of deep reflexes, pupillary and optic nerve changes, etc. Very valuable assistance is offered us by the therapeutic test, namely, toleration of mercury and KI with manifest improvement of the patient's general as well as local condition under their administration.

The average case of syphilitic involvement of the inner ear and eighth nerve does not present itself to the otologist with the diagnosis ready made. The history is often meagre; the patient, if it is a child, is brought by the parents and the guilty party rarely suspects the true nature of the trouble, and is less anxious to confess it. In both the congenital type of syphilis affecting older individuals where they are capable of supplying their own history and in the acquired form the history of syphilis is withheld or a history of catarrh is given. It might be added that in the majority of such cases which I have been called upon to treat, there is a history of middle ear catarrh, the patient informing us that his impairment of hearing came on after a severe cold in the head. Not infrequently the history has been that the patient had been under treatment by an ear specialist of good repute and had been treated for catarrhal trouble of the ears by Politzer inflation and other recognized forms of local treatment for middle ear catarrh. Furthermore, upon otoscopic examination the tympanic membrane may show the characteristic findings of a chronic middle ear catarrh, in that the drum membrane is considerably more opaque than normal, decidedly retracted and showing the posterior fold characteristic of retraction.

Upon making careful hearing tests, including those made with the tuning forks, involvement of the inner ear or nerve is recognized. Now these are not exceptional instances, but rather common. If not on the alert an incomplete examination could easily lead one into error where the history and otoscopic appearances are depended

upon rather than the functional hearing tests. For this reason I have come to consider the functional tests of greater value than the history and otoscopic appearances combined, for without the functional tests we are utterly helpless in locating the lesion; while the history and otoscopic appearances are as often calculated to deceive us as not, both as to the location of the lesion and its pathologic character. Accordingly, to establish an accurate diagnosis, there is need for every possible assistance in the way of a careful history taking, careful hearing and equilibrium test, carefully conducted Wassermann and therapeutic tests; besides a careful observation of the patient generally.

How are we to account for such errors in diagnosis, i. e., the mistaking of an internal ear or nerve deafness for middle ear catarrh, and how are such errors to be avoided? These are questions of sufficient importance as to deserve more than passing attention.

1. There is a considerably larger percentage of individuals who show evidence of previous middle ear catarrh by otoscopic examination than is generally supposed. This fact has been forced upon my attention repeatedly during talks to postgraduate students, when called upon to demonstrate the normal tympanic membrane. In looking over the class to find someone with a normal membrane I am only exceptionally successful. In the majority of cases, even where the history of ear trouble has been denied, the otoscopic findings contradict this denial, and in many cases to a very marked degree. Furthermore, the otoscopic picture in those cases coming to us for the treatment of impaired hearing does not always correspond to the patient's statement; for we not infrequently find evidences of marked changes in the membrane with quite normal hearing and vice versa. In other words, the changes in the appearance and behavior of the membrane is far from an actual index of the changes present in the tympanic cavity generally and the amount of hearing function.

This is equivalent to saying that the otoscopic appearances of middle ear catarrh, in spite of a negative history and normal hearing function, are quite common; furthermore, the otoscopic appearances of middle ear catarrh may be a mere coincidence in any case of syphilis of the inner ear and nerve, and may therefore mask the more important syphilitic conditions.

2. From the pathologic study of the temporal bones in syphilitic children, the percentage of middle ear catarrh is recognized as predominating to a greater extent than in the case of nonsyphilitics. Besides, it is accepted by all authorities, founded on clinical evidence, that syphilitic children are more prone to catarrh of the middle ear than the nonsyphilitic, probably because of the lower resistance. Granting, therefore, that the evidence of middle ear catarrh, based upon the otoscopic appearances, is much more prevalent than is generally accepted in otherwise normal individuals, it must be conceded that the evidences are even greater among the syphilitics.

3. It is reasonable to accept the view, already expressed, that catarrhal inflammation of the middle ear tends to excite a syphilitic process in the environs of the middle ear. This view is acceptable to me since my experience shows that in cases of bilateral deafness from syphilis of the inner ear, the greatest impairment of function is more often on the side presenting the greater otoscopic picture. This may be contested on the ground that in a given case with both inner ear and nerve affected to the same degree, we would naturally expect to find the hearing reduced more on the side showing the greater disturbance in the middle ear. If this is the explanation, then we would expect to find the bone conduction longer on the side showing the greater middle ear involvement, when in fact the contrary has usually been the case. All of which shows the importance of careful functional tests.

4. Errors in diagnosis are made by depending too much upon the history and otoscopic appearance pointing to middle ear catarrh and too little upon the functional tests. That mixed conditions, syphilitic involvement of the inner ear and nerve combined with chronic catarrh or suppuration of the middle ear do exist otologists everywhere accept. In such a case the unwary otologist who is accustomed to putting more reliance in the history and otoscopic appearances than in the functional test findings is apt to overlook the inner ear and nerve conditions and satisfy himself with the diagnosis merely of the middle ear condition. The more striking the otoscopic picture is of middle ear catarrh, the more likely is the attention to be focused on that alone, while the chances of detecting the inner ear and nerve affection are proportionately diminished.

Those who are accustomed to considering every phase in the case,

including most careful functional tests, before making a diagnosis, could cite many instances where a previous man in the case had overlooked the more important and graver inner ear condition.

In taking the history of the average case that comes to the otologist for impaired hearing, it rarely occurs to him to include a history of the patient prior to his present illness, important though it be, much less the family history. Furthermore, the average patient resents it, especially when it deals with the question of venereal infection. The more so, if the patient happens to be an unmarried woman. Our object should be to obtain the most information bearing on the family and personal history of the patient with the least amount of offense, otherwise we are liable to get a pert *réply* and not see the patient again. In some cases it is an easy matter to obtain an accurate history and in others quite difficult.

I find it much easier to obtain the information desired by sending the patient to the laboratory for a Wassermann blood test. On the other hand, there are a few who object to the extra cost, but they are not to be found among those who are profoundly deaf or those who have been elsewhere without relief.

Otologists generally do not think of the Wassermann test as a routine measure in every case coming to them for the treatment of impaired hearing, nor does it seem necessary excepting in those cases in which the hearing and equilibrium test show involvement of the inner ear and eighth nerve. In all such cases a Wassermann should be made as a routine measure. Furthermore, it should be made in all those cases of middle ear affections where the hearing is found to be reduced below that allowable for uncomplicated middle ear disease and where the suspicion of complications in the inner ear and nerve has been confirmed by the tuning fork and vestibular tests. Where the suspicion warrants it and where the Wassermann test made from the blood has been found negative, the spinal fluid should be examined from every angle. In spite of a negative Wassermann, the pathologic changes in the inner ear and nerve, responsible for the reduction in hearing, may nevertheless be syphilitic. Finally, we have the therapeutic test left us. Unfortunately, this is not very reliable in cases of very long standing. Recent experiences, however, have taught me to anticipate improvement after a longer period than I was previously inclined to accept.

We have gradually narrowed the question of diagnosis down to that which may be learned through an examination of the functions of the inner ear and nerve, which is not the least interesting feature of the subject.

The inner ear performs two distinctly different functions; one has to do with hearing, and the other with equilibration. Both are ascertainable to a degree by well recognized and acceptable tests.

The normal perception of sound is performed through the operation of a normal conducting apparatus (external canal eustachian tube, tympanic membrane, middle ear including the ossicles and the two labyrinthine windows) and a normal perceiving apparatus (osseous and membranous labyrinth, cochlea, nerve, nuclei and nerve paths to the centers in the brain).

Our position in space while at rest and our sense of motion in straight lines is perceived by the macula acustica utriuli and macula acustica sacculi located in the two sacs; while our sense of motion in curved lines is perceived by the three cristae ampullares in the three semicircular canals and their nerve paths to their centers in the brain.

To ascertain the hearing function, many tests, some relatively simple and others more complex, have been devised. To avoid consuming too much space on this subject, I will mention only a few of the more important, which at the same time give us the most valuable information. To begin with, every diagnostician must be thoroughly familiar with the tools he uses.

Given a case of impairment of hearing from no matter what cause, naturally the impairment is recognized by tests of the hearing to conversational and whispered voice, the watch or other mechanical or musical contrivance designed for the purpose.

Impairment of hearing may be unilateral or bilateral and its degree can be determined more or less by such methods; however, they do not tell us anything about the character of the lesion that caused it. Neither does the history or the otoscopic appearance, as pointed out elsewhere, nor does a combination of them give us certain information. There are tests, however, that do, and do so independent of other data. I refer to the Weber, the Schwabach, the Rinne tests. Additional tests for high and low tones are not indispensable in localizing the lesion.



The Weber test (tuning fork applied to middle of forehead) made with a well designed, weighted fork, lateralizes, in the case of unilateral inner ear or nerve trouble to the normal side; in the case of bilateral inner ear or nerve deafness to the better hearing ear and is heard for a shorter time than by a normal individual, used as a control. It is well to estimate the amount of shortening as definitely as possible by timing it with a stop watch. This is important, for by comparing future tests made after the same manner, one is afforded a valuable guide as to whether the case has improved or retrograded.

The Schwabach test, that is, the comparison of the patient's bone conduction with the normal used as a control. In the case of suspected inner ear or nerve involvement, the solid end of the vibrating fork is applied to the patient's mastoid on the side to be tested. After he ceases hearing it, it is applied to the control, and the difference in bone conduction is timed in seconds. In inner ear and nerve deafness the bone conduction is thus found to be shortened.

The Rinné test is made by comparing the bone conduction over the mastoid of the ear to be tested with the air conduction. In measuring the air conduction care should be exercised to place the branched end of the tuning fork at a definite distance from the meatus and always in the same manner, otherwise confusion is likely to follow.

Before making the test, the examiner should be well acquainted with the normal Rinné made with the particular fork he uses after repeated experiments upon normal ears. The Rinné test is designated positive when the air conduction exceeds the bone conduction, i. e., when it is heard for a longer time suspended in the air a short distance from the meatus than when applied to the mastoid process. The Rinné is designated negative when the opposite condition is found, i. e., shorter air than bone conduction. In normal individuals the Rinné is positive; furthermore, it is generally positive in inner ear and nerve deafness. One notable exception is in the case of pronounced unilateral nerve deafness, when it may be neutral or negative because of crossed bone conduction. In bilateral inner ear or nerve deafness with normal conducting apparatus it can never be negative. It, of course, is neutral in all cases of bilateral complete deafness, since the patient can hear neither through the air nor through the bone.

Summarizing then in the case of inner ear or nerve deafness from

sypilis or otherwise, the Weber test lateralizes to the better hearing ear. The air conduction is shortened, the bone conduction (Schwabach) is shortened, and the bone conduction is shorter than air conduction (Rinné positive). These findings, with the exception noted above, therefore, establish the lesion as one located in the inner ear (cochlea) or its nerve according to all accepted authorities.

The next question to settle is to what extent, if at all, is the remaining part of the labyrinth (the saccule, utricle and semicircular canal) involved. To be brief, the normal individual should be able to stand erect, with eyes closed, without undue swaying. He should be able to walk in a comparatively straight line forward and backward with eyes closed, making due allowance for natural clumsiness in certain individuals. To be normal, an individual should be able to look straight ahead of him at a distant fixed object without manifesting any unintentional eye movements. When movements do occur and are repeated at more or less regular intervals, and after a definite manner, the condition is recognized as nystagmus, and depending upon its character (undulatory or rhythmic), its plane of motion (horizontal, rotary, etc.) and its direction (to the right or left, etc.), a tentative diagnosis as to the location of the lesion responsible for it can be made.

The presence of a rhythmic nystagmus when looking straight ahead is more than presumptive evidence of a lesion in the static labyrinth or the vestibular nerve. Characteristic of inner ear or eighth nerve lesion involving the vestibular branch there occurs a rhythmic nystagmus to the side opposite the lesion if one side alone is affected, or to the side of the lesser loss if both sides are involved.

Normal individuals react to turning in a so-called turning stool after a definite manner and for a definite period. With the head erect, normal individuals who have been turned around ten times 3600 degrees will manifest a horizontal nystagmus to the opposite side to which they have been turned. This after turning nystagmus gradually diminishes in intensity from the moment it first shows itself until it finally stops after about 24 seconds. Besides, the so-called after turning nystagmus in normal individuals endures for a like period on the two sides when tested separately. A diminution in the duration of the after-nystagmus to either side indicates a diminution in the function on that side; for instance, an after

turning nystagmus to the right of ten seconds' duration following turning to the left indicates a diminution of the function in the right static labyrinth. Furthermore, the diminution in the duration of after nystagmus corresponds in a measure but not altogether to the amount of lost function, for some of the after nystagmus is borrowed from the normal side.

Normal individuals will react to cold water applied to one or the other ear after a definite manner. This is known as the caloric test. There are many ways of conducting the test but the preferred one is with cold water applied to the ear to be tested while the patient sits erect. After this manner and after a sufficient amount of douching with cold water the patient will manifest a rotatory nystagmus to the opposite side. If this reaction fails after repeated trials, there is evidence of loss of function on the side experimented upon. This test is not quantitative and too much reliance is not to be placed in it except where the examiner understands thoroughly the technic, acquired only after a wide experience guided by an expert. I say this advisedly, for in the cases where mistakes in diagnosis have occurred, it happened in those cases where too much reliance has been placed in the value of this test and where the technic was faulty. The mistakes I have witnessed were made by most excellent men.

An absent caloric reaction on one side with a positive reaction on the other from the same amount of water used and at the same temperature would indicate the presence of an internal ear or nerve lesion on the side where the reaction was negative.

Normal individuals react to galvanism after a definite manner. When the cathode is applied to the tragus or external canal of one ear with the anode applied to some distant part, say the hand of a patient, a current strength of 4 ma. or thereabouts produces a mixed rotatory and horizontal nystagmus to the same side. With the anode applied to the ear, the same current strength (4 ma.) produces a nystagmus to the opposite side. Thus the anodal and cathodal reaction balances on the same side and like polarities balance on the two sides. Deviations from this normal indicate a pathologic condition.

For instance, if it takes more than the amount of current strength to produce a reaction, we have an indication of diminished function, the more so if the other side reacts to a much weaker current. Thus

if the right ear reacts with the cathode to a current strength of 4 or less than 4 ma., while the left reacts only after the application of 7 or 8 ma., there is evidence of diminished function in the inner ear or nerve on the side requiring the stronger current.

If the right ear reacts to a current strength of 4 or less than 4 ma. with the cathode while the left ear does not react at all with a current strength of 12 or 14 ma., there is evidence of complete loss of function in the nerve.

The galvanic test is too big a subject to take up in detail at this time. Besides, I have covered it quite thoroughly elsewhere and recently. In brief, I may say that the galvanic test is the only one ever attempted as a differential diagnostic measure to distinguish between inner ear and eighth nerve lesions.

It has long been recognized that when the inner ear is destroyed from any cause, the eighth nerve continues to react to electric stimuli. In the case of eighth nerve destruction the reaction is negative with the electrode applied to the ear of the affected side. No amount of current strength up to 20 ma. will produce nystagmus. Above that strength it has not been tried, since 20 ma. is about the limit of toleration for most individuals.

Summarizing from the side of the static labyrinth and the vestibular nerve we find in the case of diminished or lost function, if limited to one side that spontaneous nystagmus is present to the side away from the lesion. If the condition is a fairly recent one, this nystagmus is associated with vertigo. But vertigo belongs properly to the history of the case. In a bilateral lesion, if nystagmus is present, it is toward the side where the loss of function is the less. In bilateral cases of equal intensity nystagmus is not present. Afterturning nystagmus is diminished on both sides in unilateral cases, but diminished to a greater degree on the side corresponding to the lesion. In the case of bilateral lesion the diminution is perceptibly greater to the side corresponding to the greater loss of function.

Bilateral diminution or complete loss of hearing when found to be due to a lesion of the perceiving apparatus as determined by carefully conducted functional fork tests speaks decidedly for the diagnosis of syphilis.

Bilateral diminution or loss of the so-called vestibular function as

determined by the turning, caloric and galvanic tests, likewise speaks for syphilis.

Bilateral diminution or complete loss of hearing function from a lesion in the perceiving apparatus combined with bilateral diminution or loss of vestibular function speaks for syphilis.

Pronounced loss of either function on one side with but moderate diminution of function on the other speaks equally strong for syphilis.

A greater loss of the hearing than the vestibular function is the rule in syphilis, although the opposite condition has occasionally been observed. I can recall two such cases in my own experience.

Herewith follows the report of some interesting cases of syphilis which I have had the opportunity of studying clinically during the last few years. They are presented more for the purpose of bringing out the points raised for diagnosis. These cases are selected from many cases of syphilis of the inner ear and eighth nerve that I have had occasion to treat during the past seven or eight years:

CASE 1.—W. L. B., male, thirty-one years of age. Referred to me by Dr. G. H. Wells, of Philadelphia, June 4, 1913. He is about 5 ft., 9 in. tall and weighs 130 lbs. The family history is negative. Personal history that of a chancre about twelve months ago, followed a month later with a secondary skin eruption, falling of the hair and sore throat, for which the patient had little or no treatment. At the time he presented himself to me for treatment, he complained of subjective noises in the right ear, obstructive breathing through the right side of the nose, especially in damp weather, impairment of hearing in the right ear, occipital headache, more especially during the last six months. He complains mostly, however, of vertigo. The attacks are very severe and last for several minutes at a time, during which the patient is compelled to seek the recumbent position. During the attacks the patient feels a sensation of falling and of objects moving before his eyes, but he is unable to recall in which direction the objects seem to move.

Functional hearing tests revealed marked diminution of hearing to the conversational voice on the right side. The whispered voice and acoumeter was heard ad conchum on the right side. On the left side conversational voice was heard fairly good, but diminished; both the whispered voice and acoumeter were reduced to one meter distance. The Weber (fork) test was lateralized to the left side. The Schwabach (bone conduction on the mastoid) was considerably shortened on the right and slightly shortened on the left side. The Rinne was negative on the right, positive on the left side. Hearing for both high and low tones was markedly shortened on the right and slightly shortened on the left.

*Otoscopic Examination of the Right Ear.*—Membrane was slightly opaque and slightly retracted. Hammer handle foreshortened; short process somewhat promi-

nent. Posterior fold (pathologic) was present. Mobility with a Siegle apparently normal. Membrane moved with Politzer inflation quite normally.

*Otoscopic Examination of the Left Ear.*—The findings were the same in character as those found in the right ear, suggesting a previous attack of acute secretory catarrh, but they were evidence less pronounced than in the right ear.

*Rhinoscopic Examination.*—Marked deviation of the septum to the right, obscuring a view of the middle fossa, hyperplasia of the middle turbinate on the left side with secondary sclerosis.

Mouth and throat examination revealed a rather high palatal arch, teeth in good condition, faucial tonsils quite small and submerged, no deposits in the crypts, slight secondary catarrhal pharyngitis.

From the side of static labyrinth and vestibular nerve the following findings were elicited: pronounced mixed horizontal and rotatory nystagmus to the left when looking to the left, less pronounced when looking straight ahead, and a mere trace of the nystagmus to the left when looking to the extreme right. This spontaneous nystagmus appeared to vary from day to day, but was more or less evident for many months following his first visit and even after marked improvement of his symptoms had begun.

*Reactions from Turning.*—After ten turns to the left, with the head erect, there was manifested a horizontal nystagmus to the right, of short excursions lasting about eight seconds. After ten turns to the right, with the head erect, horizontal nystagmus to the left, or, rather an increase of his already existing nystagmus to the left side, lasting 15 seconds. It was noted further that the nystagmus produced by turning was more intensive and at longer excursions to the left than it was to the right.

*Reactions from the Galvanic Tests.*—On the right side with the cathode 11 ma. there resulted a change in the existing nystagmus which was spontaneous and directed to the left, to the slightest degree of nystagmus to the right (?). With the anode 3 ma. there resulted an increase in the existing nystagmus to the left. On the left side with 2 ma. there occurred an increase in the existing nystagmus to the left. With the anode 8 ma. the existing nystagmus to the left became nil. Owing to the patient's poor physical condition and the distress caused by the examination thus far made, further examinations were deferred until the next visit.

The patient was put under mercurial inunctions and told to report a few days later, when further examination of the hearing revealed the same character of findings as on the first visit with the slightest amount of improvement—barely perceptible. Likewise, the findings from the vestibular apparatus and nerve revealed about the same findings as on the first visit. The patient was kept under antiluetic treatment—thirty inunctions followed by KI in milk t.i.d. after meals. In the meantime the mechanical faults in his nose were corrected by operation. His headache improved after three months and the patient returned to his former doctor, from whom I received the report that the patient was doing nicely. He was not seen again for a detailed examination until November 22, 1913, when he reported that his hearing was very much better; subjective noises diminished, however, they were still present. The vertigo had almost disappeared. He still suffered mild attacks of momentary duration, produced by any sudden movement of the head.

The functional hearing test showed marked improvement in the right ear to conversational voice, whispered voice and acoumeter. The hearing function on the left side was normal. The Weber test did not lateralize to either side. The bone conduction was but slightly shortened on both sides. The Rinné test was still negative on the right and positive on the left. The hearing for high and low tones was slightly below normal on the right side and quite normal on the left. Turning tests revealed slight improvement in the length of the after-turning nystagmus. The horizontal after-nystagmus was 13 seconds to both sides. Likewise, the galvanic test showed corresponding improvement. From then on until February, 1914, the patient steadily improved. He claimed that the noises had almost completely ceased, the hearing had materially improved and the dizziness was much diminished, occurring but once in a great while, and then but very mild, lasting for a short time (momentarily). He was referred back to Dr. Wells with a favorable report. The last time the patient was seen was in October, 1917, at which time he reported that he was doing very nicely, had practically no subjective noises and no dizziness. The hearing showed improvement to all tests. Bone conduction on the right side was normal. Rinné unquestionably negative and air conduction slightly shortened. On the left side the findings were practically normal. From the vestibular side there was no nystagmus present when looking straight ahead.

#### SUMMARY OF CASE 1

This was evidently a case of pronounced right inner ear and eighth nerve involvement from syphilis in the late secondary or early tertiary stage. Although I did not see the patient until a year after his initial lesion, from the history I gathered, the ear condition was present at least six months prior to my seeing him. The evidence of a mild catarrhal infection of the middle ear modified in a measure the fork test findings. A Wassermann was not taken in this case because at the time the history was so clear and the improvement so pronounced from the antisyphilitic remedies used that it was hardly felt necessary; however, I feel that a Wassermann at this time would be of considerable value from the prognostic point of view and shall recommend it the next time I see the patient. Unfortunately, he is neglectful of his condition and reports at very wide intervals.

Whether the case cited is one of syphilitic involvement of the eighth nerve alone or combined with involvement of the labyrinth is a question difficult to answer. However, the galvanic findings tell us that the nerve at least was involved. Furthermore, it tells us that at one time the function was almost completely destroyed. We are able to conclude from this case that syphilitic involvement of the

eighth nerve and labyrinth is fairly amenable to treatment even when instituted at a late period.

CASE 2.—George L., age fifty-two years. Occupation, huckster. Referred by Dr. Best, of Philadelphia. First seen April 2, 1912. Family history unobtainable.

*Personal History.*—About eight weeks previous the patient was taken with a severe attack of vertigo while eating his supper. The attack came with a clicking sensation which the patient referred to the right side of the face. The dizziness was so pronounced that he thought the room was going around and he fell off his chair. He has been dizzy ever since and staggers as if he were drunk. A few minutes after the clicking sensation the patient was given a drink of water. The water ran out the right side of his mouth. The following morning, while looking in a mirror, the patient observed that his face was crooked and that he could not shut his right eye, nor has he been able to close it well since. The night of the second day the patient noticed a buzzing sound in the right ear and this buzzing has continued ever since. He claims that he does not hear well with the right ear. He has no pain in the head or face. He complains mostly of a sickening condition which at times increases to such an extent that he vomits. He complains also of double vision. He has a fair appetite and feels strong. Prior to this present attack the patient claims to have heard normally with the right ear. He furthermore claims to have rheumatism, for which he used horse liniment.

The hearing test shows on the right side marked diminution of hearing to the conversational voice, nil to whispered voice and to the acoumeter. Weber lateralized to the left. Bone conduction very short on the right side and quite normal on the left. Rinne positive on both sides. Hearing for high and low tones markedly shortened on the right side, practically normal on the left. In looking to the left, mixed horizontal and rotatory nystagmus to the left side quite pronounced. In looking straight ahead, fairly pronounced. In looking to the right, nil.

*After-turning Nystagmus.*—After ten turns to the left, with head inclined forward, rotatory nystagmus to the right, seven seconds. After ten turns to the right, with head inclined forward, rotatory nystagmus to the left, fifteen seconds.

Testing for absolute deafness with a three-meter speaking tube in the right ear and the noise producing apparatus in the left ear, the patient was unable to recognize conversational voice. With the speaking tube in the left ear and noise producer in the right ear, the patient was able to repeat whispered words.

*Galvanic Reaction.*—Right ear—with cathode and anode, gave no response, with a current strength of 12 ma. On the left side cathode 1 ma. increased the existing nystagmus to the left. Anode 12 ma. caused the existing nystagmus to cease.

Otoscopic examination showed the right membrane to be normal in reflex, translucency, mobility and position. On the left side the same findings.

*Rhinologic Examination.*—The septum was fairly straight, slight hypertrophy of the anterior end of both middle turbinates and no evidence of sinus disease.



*Throat Findings.*—Slight secondary catarrhal pharyngitis, soft palate more elevated on the right than the left side, mobility of the tongue normal.

Examination of the facial nerve showed complete paralysis of all branches on the right side. The left side was normal.

Examination of the eye muscles showed normal mobility. With the red glass before the right eye, left eye base showed no weakness of the eye muscles ascertainable in spite of the patient's claim of double vision. Weakness of one or more of the ocular muscles may have existed at some time prior to this examination.

The patient acknowledged having contracted syphilis many years before but was uncertain as to the exact time; however, he stated that it was more than twenty years ago. Allowance should be made for the accuracy of the patient's statement, as his intellect was considerably below normal. The blood pressure taken at different times ranged from 150 to 180 systolic.

The patient was put on antisyphilitic treatment under which he improved considerably, so that by July 25 his dizziness had completely disappeared except in the mornings when first getting up. He claims that his hearing has improved considerably; besides, all subjective noises had ceased.

Functional hearing tests at this time show hearing to conversational voice, whispered voice and acoumeter improved, Weber still lateralized to the left, bone conduction on the right side, though short, was longer than on the first visit, on the left slightly shortened, Rinne slightly plus on the right, decidedly plus on the left. Hearing on the right side for low tones slightly short, and for high tones quite short. The hearing on the left side for both high and low tones was a trifle short.

*Test of the Vestibular Function.*—After ten turns to the left, with the head erect, horizontal nystagmus to the right, twenty-three seconds. After ten turns to the right, with the head erect, horizontal nystagmus to the left, twenty-three seconds. After ten turns to the left, with the head inclined forward 90°, rotatory nystagmus to the right, twenty-one seconds. After ten turns to the right, with the head inclined forward 90°, rotatory nystagmus to the left, twenty-two seconds.

*Galvanic Reaction.*—Right side: Cathode 11 ma. produced rotatory nystagmus to the right; anode 8 ma. produced rotatory nystagmus to the left. Left side: Cathode 8 ma. produced rotatory nystagmus to the left; anode 11 ma. produced rotatory nystagmus to the right.

During the course of the treatment, this patient was rather neglectful in reporting; however, opportunity was afforded to make repeated examinations at long intervals, so that I have records of examinations having been made during a period of four months only, when I lost sight of him entirely and have not seen or heard of him since.

#### SUMMARY OF CASE 2

A summary of his case would indicate that the patient had multiple neuritis involving the seventh nerve on the right side and the eighth nerve, both branches, on both sides, more particularly the

right. As a further evidence that syphilis was probably behind the condition was the marked improvement obtained through antisyphilitic treatment. The condition of both branches of the eighth nerve improved sufficiently on the left side to bring the function quite up to normal, and on the right side to somewhat less than normal. Furthermore, there was a greater restitution of function in the vestibular than in the cochlear branch, for the duration of the after turning nystagmus to the two sides at the last examination was practically normal. The suddenness of the attack and the completeness of the loss of function would suggest that if it was a neuritis, it belonged to that class mentioned by Urbanschitsch as the *typus apoplectiformis*. That there might have been an associated hemorrhage in the internal auditory canal is quite conceivable and the resulting improvement could have been due to the later absorption of the blood. Granting this as a possibility in accounting for the suddenness of the attack, there is little doubt but that the hemorrhage was merely an incidental factor in the case and not the whole cause of the patient's symptoms, for we find that the function in the left eighth nerve became disturbed subsequently to his first visit and improved under the administration of mercury and KI, so that from the history, the Wassermann, and the therapeutic test, we must accept the condition as a polyneuritis of syphilitic origin (*polyneuritis cerebialis menieriformis* of Frankl-Hochwart).

CASE 3.—Miss M. W., age thirty-four years. Occupation, nurse. Was referred by Dr. Christine, of Philadelphia, February 17, 1915. Little of importance could be gathered from the family history.

*Personal History.*—Present condition began two and one-half years ago after catching cold through washing the head and sitting in a draft of air. The following morning the patient said she could not hear a thing in either ear; the deafness was more pronounced then than at any time since. When she was attacked, she was nursing a nervous man and she thinks that her general condition of health was below par. The patient put almond oil in both ears and went out of the city, returning in about six weeks. She then went under treatment by a specialist for several months for catarrhal trouble of her middle ears. The treatment consisted of inflation of the middle ears, which she believed helped her. On closer questioning, the patient admits that she had lost her hearing in the right ear for a few days four years ago, when it returned to as good as normal. At the time of her visit to me on February 17, 1915, she complained of continual noise in her right ear, like the blowing off of an engine, with occasional noises in the left ear. She never had any discharge from either ear nor pain at any time. She complains of greater impairment in the right than in the

left ear. She feels a sensation of obstruction in the right ear as though it was filled with cotton, and at times she can relieve these symptoms somewhat by manipulation of the external ear with her fingers. She has frequent dizzy attacks, and when walking she feels as if everything was higher than should be, and she must step proportionately higher. Occasionally, when standing, sitting, or even when lying down, she feels as though she would fall; however, she never has. Upon noticing macular cornea and questioning her about them, she told me that fifteen years ago both eyes were inflamed for six months. She further claims that she is subject to colds in the head and that the right side of her nose stops up easily. She had her nose treated by the specialist when she was treating for her ears. Can not recall ever having headaches. Her general condition of health was good with the exception that she suffered with palpitation of the heart upon the least exertion.

*Functional Hearing Tests.*—Right side, shows she is able to hear conversational voice at 75 cm., whispered voice and acoumeter ad conchum. Left side, conversational voice 5 meters, whispered voice and acoumeter ad conchum. Weber test lateralized to the left. Schwabach considerably shortened on the right, moderately shortened on the left. Rinne positive on both sides. Air conduction considerably shortened on both sides, more so on the right. High and low tones shortened considerably on both sides, more so on the right.

Otoscopic examination reveals normal findings. Membranes intact, brilliant, no retraction, normally translucent, normal mobility with the Siegle and by inflation.

Examination from the side of the vestibular apparatus: no spontaneous nystagmus present when looking straight ahead. After-turning nystagmus: After ten turns to the left, with head erect, horizontal nystagmus to the right for fifteen seconds. After ten turns to the right, with the head erect, horizontal nystagmus to the left for fifteen seconds.

Rhinological examination showed a relatively straight septum; however, slightly thickened; mucous membrane somewhat swollen and pinker than normal. The general appearance was that of a recent subsiding acute rhinitis.

Mouth and throat examination revealed notched incisors and otherwise pegged teeth (Hutchinson).

Examination of the cornea showed typical deep scars in the cornea with remnants of typical brushlike lines. Characteristic of that found in acute cases of interstitial keratitis. The Wassermann blood test was negative.

The second examination was made February 19, at which time many of the tests were repeated, with practically the same findings. The patient was put on antisyphilitic treatment, and when acquainted with her condition, she became very much discouraged and disappeared, and I have not heard from her since.

### SUMMARY OF CASE 3

Summarizing this case, despite the negative Wassermann, in the presence of Hutchinson's triad, that is, the characteristic teeth, eye and ear findings, I accept the diagnosis of congenital syphilis as the

cause of her ear condition. I cite this case as one resulting from late hereditary syphilis, causing destruction of hearing. This young woman was past thirty years of age before her eighth nerve became involved. The next case that I am about to report appeared in a still older patient.

CASE 4.—Mrs. W. A. S., aged forty-seven years. Referred by Dr. J. W. Stitzel, of Hollidaysburg, Pa., October 7, 1913.

*Personal History.*—Twenty years ago the patient had an ulceration in the right eye. Two or three years after she had ulceration in the left eye, which left her with rather poor vision. Prior to three and one-half years ago she claims to have heard perfectly well in both ears. She thinks her present trouble began as the result of la grippe. At that time she believed that catarrhal trouble was the cause of her deafness. She had been under medical treatment off and on for weeks, with varying results. Sometimes she thought she was improved; then later her hearing would grow worse again. Four months ago the patient had a severe attack of vertigo, which lasted two or three days and was so severe that she remained in bed during the entire time. The vertigo was accompanied with a great deal of vomiting. During the attack she felt as though the room was going around. She had quite a number of attacks of vertigo before this, but none quite so severe. For the past four months the patient has been free of vertigo. She complains a great deal of subjective noises in both ears, which have increased in the last four months. Functional hearing test on the right side to conversational voice, whispered voice and acoumeter, nil. On the left side loud conversational voice was heard ad conchum, whispered voice and acoumeter not heard. Weber to the left side, Schwabach shortened to the right and slightly lengthened on the left. Rinne negative on both sides. Low and high tones not heard on the right. Low and high tones markedly shortened on the left. With the noise producing apparatus in the right ear and speaking tube in the left, the patient heard loud conversational voice. With the noise producer in the left ear and the tube in the right ear, loud conversational voice was heard but not recognized.

*Testing of the Vestibular Functions.*—No spontaneous nystagmus was present when looking straight ahead. After ten turns to the left, with the head erect, horizontal nystagmus to the right, twelve seconds. After ten turns to the right, with the head erect, horizontal nystagmus to the left, twelve seconds. With the head forward, ten turns to the left was followed by rotatory nystagmus to the right, lasting fourteen seconds. With the head inclined forward, ten turns to the right was followed by a rotatory nystagmus to the left fourteen seconds.

*Galvanic Reaction.*—Right ear, Cathode 4 ma., rotatory nystagmus to the right. Anode 4 ma., rotatory nystagmus to the left. Left side, Cathode 4 ma., rotatory nystagmus to the left. Anode 4 ma., rotatory nystagmus to the right.

*Otoscopic Examination.*—Right ear: Membrane opaque, retracted, moderately dull, the cone of light being less brilliant than normal. The posterior half of the membrane relaxed. The posterior fold (pathologic) was present. Left ear: Findings exactly the same as in the right ear.

Examination of the eyes revealed nothing unusual with the exception of typical deep scars in the cornea with remnants of blood vessels characteristic of a healed interstitial keratitis.

Examination of the nose showed a moderate deviation to the right with a spine along the suture line, mucous membrane on posterior end of both inferior turbinates hyperplastic; otherwise, the picture was that of a chronic simple catarrhal rhinitis.

Examination of the mouth and throat revealed typical notched incisors and pegged canines and bicuspid. Wassermann test was negative.

The patient was referred back to her doctor with the diagnosis of hereditary lues and with the suggestion that he administer KI, increasing the doses to toleration. The patient was seen at monthly intervals for a year or more, during which time there was a slight evidence of improvement. Her hearing function improved slightly, so that by October 13, 1914, one year after having first seen her, the patient was able to recognize lightly spoken words at 33 c.m. in each ear separately; however, she was still totally deaf to the whispered voice and the acoumeter. Her bone conduction was also improved somewhat. Furthermore, she was able to hear the C-4 fork on the right side which she had not heard before, and heard both high and low forks on the left side. Her after-turning nystagmus, both horizontal and rotatory, had increased perceptibly—twenty-one seconds horizontal to the right, twenty seconds horizontal to the left, sixteen seconds rotatory to the right, and eighteen seconds rotatory to the left. Her galvanic reaction was still quite normal.

#### SUMMARY OF CASE 4

Without going too deeply into the case, we may summarize from the findings herewith reported and from the records that I have that this is a case of hereditary lues based on Hutchinson's typical triad, not manifesting itself in the ears until the forty-fourth year, which is as late as any case that I have ever seen or heard of. Further points of interest are, as in the preceding case, the hearing function was disturbed more than the vestibular.

In looking over the records of this case, including those which I have not included in this report, the following points are worth emphasizing: First, that here we have unquestionably a case of syphilitic involvement of the inner ear, occurring quite late in life,—in the 44th year. Second, that the vestibular function was less involved and more amenable to treatment than the hearing function. Third, that this patient showed improvement in both the hearing and vestibular functions under the treatment with KI, begun as late as three and one-half years after the onset of her inner ear affection, is a rather encouraging factor to be considered in the treatment

of syphilis. Fourth, that the galvanic test revealed relatively normal findings, leads me to believe that so far as the vestibular apparatus is concerned, the involvement was rather in the labyrinth than in the nerve itself. This as well as the former is a clear cut case, clinically, of hereditary lues, in spite of the fact that in both instances the Wassermann was negative.

A fact worth mentioning in connection with this case and observed in others of its kind, is the prevalence of a complicating middle ear catarrh, which tends somewhat to make the complete diagnosis rather difficult, especially in the earlier stages, when the syphilitic inner ear involvement plays a smaller role in the causation of the deafness, than the middle ear catarrh. At a later stage, when the inner ear involvement becomes more pronounced, the complete diagnosis becomes relatively easier. Furthermore, I am led to believe that the middle ear catarrh in this patient's case was a predisposing factor to the syphilitic process in the inner ear. A further corroborative evidence in favor of this conclusion is the absence of nerve involvement as determined by the normal findings by the galvanic test. Many typical cases of this kind might be cited that present the same picture, but in younger individuals, between the ages of three and twenty years, many of which are to be seen in the public eye and ear clinics of any large city. It would seem unnecessary, therefore, for me to consume the space in citing them.

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## HISTORY OF CEREBROSPINAL FLUID

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**A** BODY fluid that has been studied as much as has spinal fluid, certainly repays investigation along the line of its history, the opinions held regarding it by ancient scientists, and the advances made in its study through the ages. It is impossible, of course, to attempt the complete history of such a subject in a short article. This essay, therefore, will concern itself only with the high lights in the history of this special body fluid.

### GENERAL CONSIDERATIONS

The existence of water on the brain in pathologic cases was known to the ancient. The existence of fluid in normal cases, however, does not seem to have been known to them. Hippocrates did not mention spinal fluid in his writings, although in the later Hippocratedian collection the brain is spoken of as a gland. The reference is made, not to the spinal fluid, but to the so-called secretion which was held by ancient authorities to be poured down from the brain into the pharynx. Herophilus (born 300 B. C.) knew of the existence of the ventricles and the choroid plexus, but did not know the function of the choroid plexus. This, by the way, is a matter that is unsettled even to this day. Did Herophilus who dissected hundreds of human bodies know of the existence of cerebrospinal fluid in the ventricles? It seems only natural to suppose that an observer like he was would notice the presence of a large amount of fluid in a cavity, something that one notices immediately upon cutting the brain open. Herophilus, however, describes the ventricles, which he considers the seat of the soul without making any reference to the cerebrospinal fluid. There is a possibility, that the lost books of Herophilus might have contained some such reference.

Erasistratus of Julis (330-250 B. C.) described four cavities in the brain, yet spoke of no fluid in them. Galen mentioned the choroid

plexus but said nothing of its relation to the cerebrospinal fluid. Hemesius of Emersa (born 340 A. D.) localized special mind power in the ventricle, imagination in the anterior ventricle, wisdom in the middle, and memory in the posterior ventricle, but did not speak of the fluid in the ventricles. One would naturally turn to Vesalius for a description of cerebrospinal fluid. Vesalius did observe the choroid plexus, and he must have observed the spinal fluid also. He however, devotes page after page of his work on the question of localization of the soul, without making reference to the spinal fluid.

References to spinal fluid are made in the writings of Varoli (1543-1575). This scientist, who described the pons that bears his name, denied the existence of pneuma in the ventricles. and insisted that it was fluid that was occupying the ventricles.

The conventional description of the discovery of spinal fluid is attributed to Contugno. Domenico Contugno has made many discoveries in medicine; he has discovered intestinal lesions in a post-mortem case of typhoid, and he has demonstrated albumin in urine on boiling. He it was who discovered the aqueductus Contugni or the internal ear aqueductus, and in 1784 he demonstrated spinal fluid in fishes and turtles, although he could not find it in dogs.

Although Contugno usually gets the credit for the discovery of spinal fluid, Bilanchoni claims that Valsalva saw before Contugno "an ounce of a certain liquid in cutting the cord membrane of a dog, the fluid resembling that seen in articulation."

The lack of a method by which normal spinal fluid could be demonstrated in living beings was responsible for the lack of interest in that fluid. The interest was thus confined to pathologic cases.

In 1764 Robert Whytt described tuberculous meningitis. He divided the diseases into three stages depending upon the behavior of the pulse. He attributed the manifestations to a serous exudate.

In 1768 he published his work on acute hydrocephalus, under the title "Observations on the Dropsy of the Brain." He included under acute hydrocephalus all cases of acute brain disease.

A description of spinal fluid in normal cases we find in the writings of Albertus von Haller. In his *First Lines of Physiology*, in the third Latin edition Haller says:

"The fluids which, being deposited from the blood into other vessels, are said to be secreted, seem reducible to four classes. The



first consists of viscid fluids, coagulable by a heat of about 150 degrees, by alcohol, and by strong acids; although generally, in the living animal, they escape in the form of vapor, and after death are compacted into a gelatinous substance. To this class belong the liquor and halitus of the ventricles of the brain, the pericardium, pleura, peritoneum, tunica vaginalis, amnois, joints, renal capsules, and probably of the womb, with the juices of the stomach and intestines, and lastly the lymph generally known."

And again Haller says:

"Have lymphatic vessels been seen with certainty in the brain? They have been described in the large choroidal plexus, amongst the fibers of the olfactory nerve, and in the pia mater. For my own part, I have never seen them, and it is probable that there are none, since there are no conglomerate glands in the brain, which are always found near these vessels. As for the various accounts which are given of the pituitary gland, of the infundibulum, and of the ducts which lead from thence into the veins of the head, absorbing water from the ventricles, they are not supported by any anatomic demonstration; which makes it probable that the vapor, which is secreted into the ventricles of a healthy person, is, in like proportion, absorbed again by the inhaling veins; and that if there be any excess, it descends through the bottom of the ventricles to the basis of the skull, and into the loose cavity of the spinal marrow. That this is the case, appears from the palsies, which ensue after apoplexies; and from the watery tumors in the lower part of the spinal marrow, in hydrocephalic patients."

Haller thought that the fluid is not only secreted into the hollow tubes of the medulla, but that the fluid is also continued into the small tubes of the medulla. This is a part of Haller's explanation of the mechanism of irritability, the original conception of which was brought forth by Glisson. Haller says:

"Therefore, upon the whole, it seems to be certain that, from the vessels of the cortex, a liquor is secreted into the hollow tubes of the medulla, which, being continued into the small tubes of the nerves, and propelled to their extremities, is the cause of both sense and motion. But there will be a twofold motion in that humour; the one slow and constant from the heart; the other not continual, but exceed-

ingly swift, which is excited either by sense or any cause, as motions arising in the brain."

As is seen from the above, Haller knew of the existence of cerebrospinal fluid in the ventricles, and he also mentioned the fluid descending through the bottom of the ventricles to the veins of the skull and into the loose cavity of the spinal marrow. He did not, however, give a full description of the cerebrospinal fluid and did not know the nature of it. This last part was left for another man, for Magendie. He it was who accurately described the physical appearance of the fluid, and while the communication of the fluid in the ventricles with the base of the brain by the foramen Magendie is doubted by some, Magendie had a clear-cut conception of the workings of the fluid, especially the fluid at the base of the brain. He says:

"But there is a disposition unknown to Bichat, which I have recently discovered, and which contributes in a manner extremely efficacious to the conservation and defense of the medulla.

"The canal which is formed around the medulla by the pia mater, and which is lined by the arachnoid, is a great deal larger than is necessary to contain the organ; but during life the whole interval is filled up by a serous liquid, which strongly distends the membrane and which spouts out to many inches in height from a small puncture made in the dura mater. An analogous arrangement is also to be observed around the brain and cerebellum. I have given to this fluid the name cephalorachidian or cephalospinal. It is easy to conceive how efficacious must be the protection thus derived from the liquid which surrounds the spinal marrow, and in the midst of which it is suspended like the fetus in utero; with this difference that it is fixed in its position by the ligamentum dentatum, and the different spinal nerves.

"Besides the different envelopes of the brain of which we have spoken, and the dura mater which covers it in its whole extent this substance is everywhere surrounded with a very fine serous membrane the principal use of which is to yield a thin fluid, which lubricates the brain. The arachnoid penetrates to all the cavities of the brain; and even secretes a perspiratory fluid."

As is seen from the above, Magendie knew of the presence of the cerebrospinal fluid and also the functions of the fluids, for what-



Fig. 1.—Albrecht Haller (1708-1777).



Fig. 2.—François Magendie (1783-1855).



Fig. 3.—Fritz Schaudinn (1871-1906).



ever else may be the function of the spinal fluid, it surely is also protective in nature.

A new era in the history of spinal fluid was ushered in when a method was found by which spinal fluid could be removed from the living. As early as 1856 Middeldorpf performed a cerebral puncture on the living. This operation, however, necessitated trephining of the skull and a scalp wound, and involved a number of instruments. It was Corning who first performed a spinal puncture.

Corning injected 20 minims of a 2 per cent solution of hypochlorate of cocaine into a space situated between the spinous processes of two of the inferior dorsal vertebræ. Five minutes after the injection there were marked evidences of marked incoordination in the posterior extremities. A few minutes later there was pronounced weakness in the hind legs, but there were no signs of feebleness in the anterior extremities. The Faradic current showed there was no reflex action of the hind legs but the anterior extremities responded quickly.

He then injected 30 minims of a 3 per cent solution of cocaine hypochlorate into a space situated between the spinous processes of the 11th and 12th dorsal vertebræ, in a man suffering from spinal weakness. As there was no numbness noticeable, he injected after six or eight minutes, 30 minims more in the same spot. In ten minutes the man complained that his legs felt sleepy and brush application showed that sensibility was greatly impaired. Corning suggested that there might be great therapeutic advantage afforded by such local medication in a large number of morbid conditions of the cord.

Corning unfortunately does not describe his technic nor the kind of needle used. Besides, he introduced the needle too high up in the spinal column, a place not free from danger of injuring the cord.

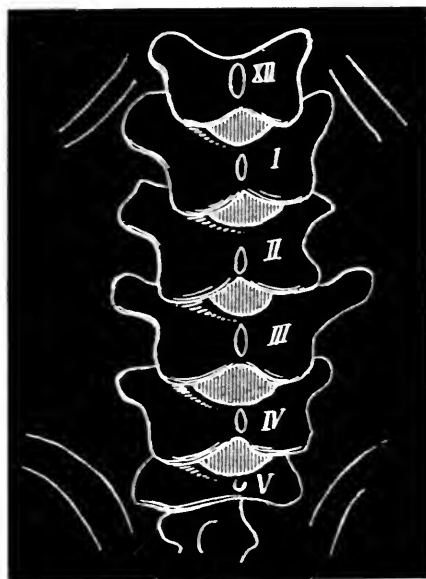
In 1891 W. Essex Winter reported the drainage of spinal fluid in four cases of tuberculous meningitis. His first case was treated by him in 1889. He made an incision in the skin of a patient suffering from tuberculous meningitis a little to one side of the spine of the second lumbar vertebra, and then introduced a Southey tube and a trocar until the point struck against the lamina. The point was then directed slightly downward and pushed through the ligamen-

tum and theca and then inclined toward the median line. On withdrawing the trocar, clear fluid rushed into the tube. A fine, India-rubber tube was then arranged for continuous drainage. The symptoms improved immediately, although the patient died subsequently from tuberculous meningitis. From 1889 to May 1891 he treated three more cases of tuberculous meningitis, and all of them improved for a short while although they all died subsequently.

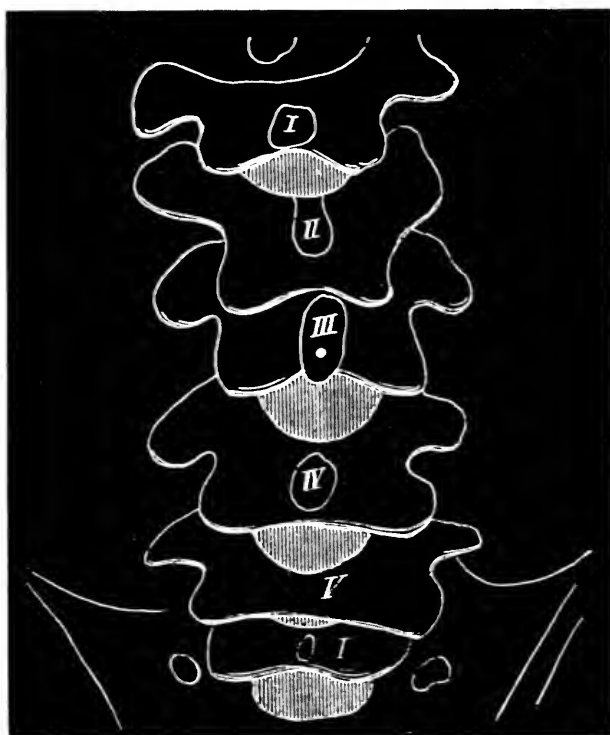
Charles A. Morton followed the method of Winter. In discussing the pathology of tuberculous meningitis with reference to its treatment by tapping the subarachnoid space of the spinal cord, Morton says: "What symptoms can be relieved by it only the practice of the operation can show; that out of four cases operated on in the Middlesex Hospital in one there should have been contraction of the unduly dilated pupils, and in another slight improvement in the general condition, is encouraging when we remember that drainage was not maintained in all the cases. The operation does no harm and as the patient is already comatose no anesthetic is required."

As is seen, he did his tapping when the patient was already in comatose condition. He does not say what technic he employed. Only at the beginning of the article he speaks of the recent procedure of tapping the subarachnoid space of the spinal cord in cases of tuberculous meningitis, which would indicate that he followed the method of Winter; namely, an incision of the skin of the lumbar vertebra, a big trocar, and a continuous drain.

While others before him performed spinal punctures and spinal drainage, it is Quinke who deserves the credit for the simplification and perfection of the spinal puncture. It is true that Corning performed the puncture before Quinke. His operation, however, was fraught with danger to the cord, the point of introduction being too high up in the spinal canal. Winter did his puncturing in the lumbar region but he used a large trocar, a continuous drain and made a large incision of the skin. Quinke used a plain needle and he so perfected his technic that very little can be improved upon even to this day. At the Tenth Congress for Inner Medicine Quinke reported two cases of hydrocephalus that were treated by withdrawal of spinal fluid; the first case was a chronic hydrocephalus in which the fluid was removed by trephining and in which the contractures of the extremities and the contracture of the neck disap-



(A)



(B)

Fig. 4.—Drawings accompanying original article on spinal fluid by Quinke. *A* represents lumbar region of skeleton of a one-year-old child. *B* represents lumbar region of skeleton of a six-year-old child.





peared afterwards. The second case was one in which a lumbar puncture was done and in which the child greatly improved. Quinke, therefore, advised the use of spinal puncture for therapeutic purposes in cases of marked cerebral pressure, especially in tuberculous and in acute hydrocephalus. Not only did Quinke describe the technic of spinal puncture but he also measured the pressure of the fluid, and determined some of the chemical composition of the fluid.

For two years no reports appeared in the literature regarding spinal puncture, when Lichtheim called attention to this procedure as a valuable aid in diagnosis, and two years after that (in 1895) Fubringer wrote a report of 107 punctures done in 80 cases. In America Browning reported spinal punctures in 1894, and G. W. Jacoby reported over 30 punctures in 1895 and 1896. Since that time spinal puncture has become a routine diagnostic and therapeutic procedure with every physician.

A new angle in the history of spinal fluid was opened up with the speculation as to the source of this body fluid. In 1853 Faivre advocated the idea that spinal fluid is a secretion. The first direct evidence that the spinal fluid is a secretion was furnished by Petit and Girard in 1902 who described changes in the cells of the choroid plexus after pilocarpine and muscarine. Many pages would have to be written if one wished to bring the pro and con evidence in this phase in detail. Suffice it to say that the source of spinal fluid has become a matter of great scientific research, and at present we have a number of theories, the following of which are the most important:

1. The theory of Magendie that it is protective in nature.
2. The theory of Gaskell that it is a primitive digestive juice.
3. The theory of Dandy that the choroid plexus fulfills the functions of an intracerebral gill and that the spinal fluid is concerned in respiration.
4. The theory of Petit and Girard that the fluid has an internal secretion.
5. The theory of Mott that the cerebrospinal fluid as it circulates in the perivascular and pericellular channels, may give up water and carbon dioxide and take up oxygen and sugar.
6. The theory of Halliburton who considers cerebrospinal fluid

a Locke's modification of a Ringer's solution which bathes the neurones.

7. The theory that it serves as a destroyer of toxic substance.

8. The theory of Mestrezat that it is a dialysate of the plasma on specially differentiated epithelium, analogous with the aqueous humor of the eye.

Bacteriology, serology and chemistry could hardly pass this great fluid without leaving their impress on it. There is not a discovery in bacteriology that does not bear direct relation to the history of spinal fluid. The discovery of the tubercle bacillus by Robert Koch changed the name and the conception of acute hydrocephalus to tuberculous meningitis. The discovery of Leichtenstern in 1885, of intracellular diplococci which was later worked out with great accuracy by Weichselbaum in 1887, changed the name "spotted fever" and "epidemic cephalalgia" to meningococcus meningitis, and the discovery of pneumococcus by Fränkel introduced system into the chaos of suppurative meningitides.

One of the greatest advances in our knowledge of spinal fluid was made in connection with the study of syphilis, and the study of spinal fluid has in turn greatly enriched our knowledge of syphilis. Schaudinn's discovery of the spirochete pallida, Bordet's discovery of complement fixation, Ehrlich's work on immunity and Wassermann's serologic test found no other body fluid to which the principle could be applied any better than the spinal fluid. It is admitted by all who are familiar with the subject that the spinal fluid Wassermann is positive at the very early stages of luetic involvement of the central nervous system, at the time the blood Wassermann is still negative. This makes the Wassermann on spinal fluid one of the earliest and best guides in the diagnosis of syphilis.

Chemistry has influenced the spinal fluid as it did all other body fluids, although the effect was not as beneficial to the human family as was that of bacteriology. True enough, we have the globulin tests to diagnose syphilis of the nervous system, and the presence of meningitis, but as yet no therapeutic benefit could be attributed to the chemistry of spinal fluid.

Serology, on the other hand, has done a great deal in the therapeutic line in connection with spinal fluid, the most marked achievement in this connection being the discovery of the antimeningococ-

cic serum by Flexner and Jobling. It is still too early to speak of any benefit attained from pneumococcic serum or influenza serum, just as it is premature to judge of the historical importance of intraspinal antisyphilitic medications. Present indications, however, lead one to believe that there is a great future awaiting intraspinal therapy.

Finally, the new offspring of modern science, physical chemistry, is making its impress on the history of spinal fluid. The H-ion concentration, the cataphoresis, the Lange colloidal gold test and various precipitants based on physicochemical characteristics are earmarks in the history of spinal fluid.

In short, the history of spinal fluid is the history of modern medicine in all its phases.

## PARASITOLOGY AND SEROLOGY OF SYPHILIS\*

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### PARASITOLOGY

THE causative agent of syphilis, after many years of activity shrouded in obscurity, made all the more impenetrable by numerous repeatedly unsuccessful attempts to discover an organism for this disease, finally came to light in the shape of a delicately spiral organism. That this discovery came about through application to the problem of a highly specialized zoological training, is a tribute to the efficiency of present-day scientific methods of research. Contrasted with the earlier, incomplete, and inaccurate observations by previous investigators in this field, and there were men of prominence among them, whose word carried weight in the scientific world of those times, the success of this final achievement illustrates once more the great truth that important discoveries are not the result of accident, but rather the reward of systematic research, founded on precise methods and accurate preparation.

It is not necessary at this late date, to read a brief, in order to establish this organism's claim to specificity. Its presence has been demonstrated in every lesion of acquired and congenital syphilis. It has been grown in pure culture on artificial media outside the body. Characteristic lesions have been produced in animals by inoculation with these cultures and from these lesions so produced the organism has been recovered in pure state of cultivation. Many of the problems on which it was hoped the discovery of the organism would finally throw light, have remained, however, no nearer solution than before. One of the first difficulties encountered, that of giving the organism a name, is still unsettled.

### NOMENCLATURE

The name "*Spirocheta pallida*," suggested at first, by its discoverer, and adopted at once by everyone, will perhaps never be

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entirely discarded. Schaudinn himself, however, was one of the first to abandon it, recognizing that it could not be maintained under the international rules laid down for the guidance of taxonomists by the International Zoological Congresses. He then offered the name "*Treponema pallidum*," which seems less objectionable under the rules mentioned, and this name is regarded today by systematists as the best nomenclature available in the light of our present knowledge of the organism. The question of name is purely one for zoologists to settle as the proper name of the organism will be based on data which they are best fitted to analyze. For the purpose of the medical man, however, whether the organism of syphilis be called the spirochete pallida, the *T. pallidum*, or some other name to be offered later, its morphology is clearly enough established to enable us to recognize it microscopically and to differentiate it from similar organisms with comparatively little difficulty. For the medical man in this country, only two spiral organisms are likely to be confused with it and they are the *Treponema microdentium* and *T. mucosum*. The *T. pertenue* can be eliminated, because we do not see yaws in this country.

#### MORPHOLOGY

Morphologically, the pale treponema is a delicately spiral organism, varying in length from 6 to 14 microns, and in width from .2 to .25 microns. The spirals are from 1 to 1.2 microns apart, sharply curved, symmetrical, and regularly arranged when viewed in stained specimens, but when most actively motile in fresh preparation, somewhat lacking in symmetry. It is pointed at both ends and sometimes terminal flagellae can be seen. As its name implies, it is practically nonrefractile and takes stains lightly, or not at all. In general the usual bacterial stains do not color the organism in dried film preparation, while most of the blood stains do. It is best demonstrated by the various Giemsa methods of staining, taking a red color against a blue or bluish red background. It may be demonstrated in film preparation, by the addition of India ink, spreading the mixture very thinly before drying, and also by impregnation with silver, according to the method of Fontana and that of Levaditi. To demonstrate the organisms in tissues, Levaditi's method by silver impregnation is the most successful.

Methods of staining, however, do not offer the same opportunity for study, nor as facile a method for recognition of the organism as the examination of fresh wet preparation with the dark-field apparatus. When viewed thus, by reflected light against a dark background, the organism stands out clearly, as does a star against a black sky. What is still more important, however, by this method the motility of the organism can be closely studied and assists greatly in the differentiation. Motility is best observed immediately after the organism is removed from an active lesion, as it soon becomes less active and ceases altogether, after a few hours at room temperature. Unlike most spirochetes, the motility of *T. pallidum* is practically continuous until it finally comes to rest. There is a spinning motion on its long axis, a forward and backward motion in the direction of its long axis, and sometimes an undulating motion. Often, very long specimens are seen having the appearance of two organisms hinged together end to end, which in moving, bend sharply at this hinged point. This phenomenon suggests a transverse division, but as phenomena suggesting longitudinal fission have also been observed, no definite conclusion can be drawn.

#### METHODS OF DEMONSTRATION

In the diagnosis of chancres, syphilitic simple erosions and erosive papules of the mucous membrane, and secondary lesions of the skin, too great emphasis can not be laid upon the importance of a dark-field examination of material from the lesion, not only from the point of view of simplicity and rapidity, but on account of the greater accuracy. Every suspicious sore, wherever it is located, can be investigated in this manner. When applied to lesions in the mouth, however, one should exercise exceptional care to avoid confusion with the *T. microdentium* and *T. mucosum*, which are so nearly identical in appearance, with the *T. pallidum*, that the knowledge of an expert is required for differentiation. This confusion may be avoided by drying the lesion thoroughly, removing all surface exudate and detritus, and using for the preparation, only the blood-tinged serum exudate, which appears on the fresh surface from the deeper part of the lesion. Such an exudate, from the secondary syphilitic lesions of the mouth, will contain many *T. pallida*. No conclusions should be based on the findings in a preparation contaminated with saliva.

This method of preparing specimens for dark-field examination should also be employed for lesions situated elsewhere than in the mouth, because it simplifies differentiation by eliminating other nonspecific spirochetes, which might be confusing, and also decreases the likelihood of missing the treponemata, which are present in greater numbers in the deeper portion of the lesion. The serum exudate, expressed from chancres, is rich in the pallida, until healing begins. After that, they diminish in number until few organisms can be demonstrated and then only after the most painstaking search. This is also often true when chancres have been treated locally with powders containing calomel. In the exudate from hypertrophied papules in the region of the anus and genitalia, *T. pallidum* is present in large numbers and must be differentiated from *S. refringens* and *T. calligyrum*. These two organisms are coarser than the pallidum, particularly *refringens* which is also longer, less symmetrically a spiral, with a different motility. Treponemata may also be demonstrated in preparations made from syphilitic macules, papules and pustules in the method described, but in these lesions they are not nearly so abundant as elsewhere.

#### VIABILITY

Chancres, moist hypertrophied papules, and open lesions of the mouth and skin are the most highly contagious lesions, because of their position and the fact that they exude a serum very rich in *T. pallidum*. Pallida are killed by drying, which explains the low infectivity of dry or closed lesions. That the pallidum may survive indefinitely in the body, is evidenced by the well known chronicity of syphilis, and is supported by the findings by various investigators of living treponemata in the scars of chancres many years after they are healed, and by the more recent investigations of Warthin<sup>1</sup> in the active and healed lesions of the viscera. Outside the body, the organism may survive in resected tissue, for 48 to 72 hours, and probably longer in some instances, but when kept in the serous exudate, rapidly loses motility and succumbs in about 24 hours. In one instance, however, Graves<sup>2</sup> successfully inoculated a rabbit with blood from a paretic after keeping the specimen in the incubator in a sealed tube for many weeks and months. He has not, however, as far as I know, been able to repeat this experiment.

For practical purposes the importance of the organism's viability

outside of the body is in its bearing on contagion, and in this respect it can be seen, as already stated, that the moist syphilitic lesions are the more dangerous because the organisms can live for hours in the wet exudate when removed from the body, but rapidly succumb to drying. In its relation to therapy, viability within the body presents a problem as yet unsolved. If we must admit as shown by Warthin,<sup>3</sup> that foci of living *T. pallida* persist during the life of a syphilitic individual, throughout the viscera and tissues in treated cases, as well as in untreated and unrecognized cases, we must abandon for the present all hope of curing syphilis. I find it difficult, however, to believe that no cases of syphilis are cured. It is probably true that treponemata acquire a tolerance for our present arsenic and mercury preparations, as shown by Akatsu<sup>4</sup> *in vitro*, but it is also true that this tolerance is soon lost when the drugs are withdrawn, and it is not transmitted to succeeding generations of the organisms. Furthermore the tolerance is specific and limited, so that by properly alternating mercury and arsenic preparations in the treatment, this difficulty should be obviated.

#### VIRULENCE

The question of variations in virulence is closely associated with that of strains. These relations have been much studied of late, since the successful and very ingenious methods of cultivating the organism on artificial media outside the body have been furnished by Noguchi.<sup>5</sup> That there are various strains, has been clearly demonstrated in cultures and by animal inoculation. Noguchi<sup>6</sup> can differentiate morphologically and clinically three strain groups in a series of 10 organisms which he has isolated. Reasoner<sup>7</sup> has demonstrated a strain from the brain of a rapidly fatal case of paresis which exhibits a highly invasive quality or selective affinity for nervous tissue, in a series of rabbits. Observations by Nichols,<sup>8</sup> Weil,<sup>9</sup> Graves,<sup>10</sup> and others, support this observation. Such a strain has been shown by Noguchi to be less virulent than those grown from chancres. From clinical observations, the existence of strains has long been suspected, but the question of virulence is so confused with individual variations in the susceptibility of patients that conclusions from this field are of little value. That animals react differently in time and degree to different strains, indicates that there is a variation



in virulence among *T. pallida*. Cultural experiments indicate only too clearly that avirulent strains can be produced.

#### COURSE IN THE BODY

The role played by immunity in syphilis presents a field for research which, comparatively speaking, has as yet hardly been touched. Its relation to the parasitology of the disease must necessarily be close. We know practically nothing of what takes place with the organism during the interval between inoculation and the appearance of the chancre, and during the periods preceding the appearance of secondary and tertiary manifestations. Some individuals exhibit greater resistance than others to the *T. pallidum*. The organism appears to have greater difficulty in overcoming inhibitory influences in certain individuals. These phenomena are expressions of reactivity on the part of the host to the organisms. The organism itself, we know, after passing the portal of entry starts early on its course of invasion, leaving behind a focus which multiplies, and finally after a period of several weeks the host marks the site with a chancre and attempts to cut off communication with the rest of its domain by sealing the lymphatic route leading from it. Then an interval ensues during which nothing but the local disturbances are manifest. Suddenly and almost on schedule time, various manifestations of the presence of the organism throughout the host become apparent and the organism makes its appearance again in force in numerous and widely scattered foci. Again the reactivity of the host asserts itself and another and much longer interval of quiescence intervenes to be followed by a third series of manifestations of their presence in much diminished numbers, in much fewer foci, but with more deadly effect.

We do not know if the *T. pallidum* is disseminated from the primary focus through the blood stream or the lymphatics or through both. We do know that they are present in both and much more numerous in the lymph. It seems reasonable to suppose that the treponemes being such fastidious anaerobes in artificial culture would not select the blood stream as a medium of choice. I have once observed *T. pallida* which had become immotile after an hour of incubation in wet preparation, exhibit the most frantic motility upon the addition of a drop of fresh whole blood from a prick in my finger. I

draw no conclusion, but the observation is suggestive in this connection. The greater difficulty in successfully inoculating animals intravenously as compared with the tissue inoculation is well known. I know of only one case of syphilis developing after transfusion, without primary and with intense secondary manifestations. This was a man with pernicious anemia in desperate condition who was transfused with the blood of his son. The donor strenuously denied syphilis and it was afterwards found that for five days prior to the transfusion he had had a syphilitic chancre. The patient exhibited secondaries six weeks after transfusion.

Whether the treponemata arrive first in the lymphatics and thence in the blood stream, or whether they pass primarily through the blood stream, I do not know. I believe, however, that they find the blood stream unsuitable, and by their motility make their way through the vessel walls into the lymphatics of the vessels and are then carried along with the vessel, emerging therefrom into the intercellular spaces to form new foci.

#### SEROLOGY

Several years ago, it was remarked that there could be no discussion of syphilis without bringing in the Wassermann reaction. More recently it has been stated that "The Wassermann reaction becomes . . . one of the best diagnostic aids known in modern medicine." I would like to say today, that no clinical differential diagnosis is complete until the patient's Wassermann reaction has been determined. I would also like to state, however, that it would be expecting too much of this or any other tests, that the results must always indicate a positive or negative diagnosis. First, because patients who are the subject of syphilitic infection and have a positive reaction, may also be the subjects of some form of disease not dependent upon the syphilitic infection. Second, because not every patient with syphilis will give a positive reaction under all conditions; and third, because various factors may enter into the reaction and constitute an error leading to a false result. The Wassermann reaction is peculiarly susceptible to errors of this sort, as well as to those resulting from imperfect technic and variation in the quality and strength of the reagents employed. This is so, particularly because of the cumbersome and complicated nature of the

reaction and because of the uncertainty in the outcome of the processes of preparing the reagents.

It is not within the scope of this paper, however, to enter into a discussion of these technical matters, but rather to treat the serology of syphilis from the clinical side with especial emphasis on the question of the interpretation of results. It is necessary, however, to point out that the value of the test clinically will vary greatly in direct proportion to the care with which it is performed and the expertness with which the various biological reagents are prepared. The peculiar property of the blood of syphilitics of absorbing complement in the presence of certain lipoidal substances, which is the underlying phenomenon in the positive Wassermann reaction, is due to some principle in the serum of these patients regarding the nature of which nothing is known. It is not only nonspecific in the sense that it is not an antibody to the *T. pallidum*, but it is not even peculiar to syphilis alone, being present also in the blood of patients who are the subjects of yaws or leprosy. Under these circumstances, it seems best to look upon the Wassermann reaction as a manifestation of the activity of these diseases, or in other words, as a symptom. When we can exclude yaws and leprosy as, fortunately, we can in this country, the positive Wassermann test becomes a symptom of syphilis that is pathognomonic.

#### INTERPRETATION OF THE WASSERMANN REACTION

In interpreting the results of the Wassermann reaction, a difference should be made according to the purpose for which the reaction is employed. It will be seen that in diagnosis, special emphasis must be laid on the importance of guarding against an erroneous interpretation, which might result in wrongly diagnosing a case syphilitic. If an error is unavoidable, it is best to err in the direction of a negative interpretation. When the test is used as a guide in the treatment, the reverse is true, and an error in the direction of a negative interpretation is likely to lead to disaster.

The positive Wassermann reaction offers the least difficulty for interpretation. In a properly performed and carefully controlled test it means syphilis, with very few and unimportant exceptions. For example, employing lipoidal extracts derived from normal tissues and fortified by the addition of cholesterol, makes the Wasser-

mann reaction much more sensitive in the direction of positive results, but this nonspecific element is never sufficient in itself to cause a complete positive with the serum of a normal individual. If we, therefore, regard as positive, only those results which represent 100 per cent fixation, the objection is overruled. Isolated cases of other diseases, notably malaria and scarlet fever, have been reported with a positive Wassermann. Here the diagnosis rests on the easily recognized clinical manifestations and microscopic blood picture, although it should not be lost sight of that syphilis may coexist in these cases. Yaws and leprosy we have already mentioned as being eliminated from consideration in this country. Of more importance may be recent reports that many tuberculous patients have positive Wassermann tests, when cholesterin fortified antigens are used. All investigators do not agree in this, however, some reporting very low percentages of positives. The frequent symbiosis of tubercle bacillus and *T. pallidum* should be borne in mind. A surprisingly low percentage of positive tubercle-complement-fixation tests were obtained in an enormous series of blood specimens from the laboratory of the Syphilis Department at the Johns Hopkins Hospital. Until much stronger evidence is adduced, I do not consider this possibility of importance in detracting from the meaning and value of a positive Wassermann in a patient who is also the subject of a tubercle infection.

Much criticism of the Wassermann test has arisen from conflicting reports when several serologists examine the serum of the same patient. One should not regard this as a fault of the reaction itself, as has been intimated on various occasions. It is almost entirely a matter of lack of uniformity in the technic and standards employed by different serologists. But even with the greatest care these discrepancies will occur when such patient's serum approaches the borderline between a positive and a negative reaction. At such a time the principle in the patient's serum responsible for the positive Wassermann may, and often does, vary in amount to a surprising degree, from day to day. Very close to this matter is another source of confusion, namely, that arising from the various systems employed by serologists in reporting results of their tests.

With the view of reporting different *degrees* of positive reactions serologists employ one or multiple plus signs, and combinations of

plus and minus signs to indicate doubtful reactions. There is no uniformity in their meaning, however. One serologist arbitrarily adopts one-plus to represent a percentage of fixation as gauged by the eye, two-plus more fixation, three-plus still more and four-plus complete fixation. Less fixation than one-plus, he reports plus over minus or minus over plus. Another serologist indicates a complete fixation with one unit of patient's serum by reporting one-plus, with half a unit two-plus, a quarter unit three-plus, and an eighth unit four-plus. Still another serologist represents by the number of plus marks the number of antigens with which a patient's serum gives complete fixation. I criticise this practice not only because of the confusion it occasions but also with regard to the amount and character of the information conveyed to the clinician.

It is well known that the degree of positiveness of the Wassermann reaction as determined by a titration of the patient's serum is no index to the extent or severity of the disease. The most virulent cases often have a negative reaction, and refractory cases may have low titre positive reactions, or easily obliterated positives which recur. Yet we constantly hear the clinician declare that his patient has a "strong Wassermann reaction," with emphasis on the "strong," indicating that he regards the patient's conditions as especially serious because the reaction was reported four-plus. A positive Wassermann reaction represented by one-plus mark, if you will, should indicate 100 per cent fixation. Then as an aid to diagnosis your positive Wassermann would mean that the patient has syphilis, and it can tell you no more. In following the progress of treated cases, multiple plus marks may seem of great value, but here again let us see how much help they afford. The greatest drop in titre of a positive serum takes place during a short period following the onset of treatment, it then drops more slowly until it becomes negative. It remains negative as long as treatment is continued and treatment must be continued a long time before hope of a cure may be anticipated. One can not speculate on the duration of this part of the treatment before a negative Wassermann is produced. Of what value then is it to know that during a brief period of time under treatment the positive Wassermann has passed through a short phase, as represented by the plus symbols four to zero. Time is the important element with regard to the Wassermann reaction in cases

under treatment; not degree of positiveness. Degree tells us nothing; time gives us an idea of resistance to treatment.

Correct interpretation of the negative Wassermann reaction is not so easy, but as already stated elsewhere in this paper, a mistaken diagnosis based on a negative serum test is not so serious as that based on a false positive. Sooner or later the patient will develop some sign or symptom of syphilis and a later test may be positive. Eliminating errors due to technic, which does not form a part of this paper, it is an unexplained fact that all syphilitic patients do not have a positive serum, and this may be so in most virulent cases. Whether rightly or not, I do not know, the tendency is to regard such cases as those in whom the syphilitic process is either not active or so intensely active as to overwhelm the patient and inhibit the process or processes leading to the production of the Wassermann positive substance. Negative serum in an early primary case may well be explained by the lack of time necessary for suitable conditions to be produced. But during the period when secondary manifestations are making their appearance, negative tests are exceedingly rare. Visceral syphilis, the so-called latent type, and the treated or possibly cured cases form the largest group of negative cases. They also represent the group in which a diagnosis of syphilis is made most difficult by the absence of clinical signs. It might well be that all the positive Wassermanns in this group belong to the cases with active visceral lesions, as illustrated by the frequency with which cases of aortitis respond with a positive Wassermann test and that the remainder are the true latent cases. The findings of Warthin are significant in this particular and support this interpretation. The action of mercury and the arsenobenzol preparations by their treponemocidal action limit or remove the active disease and tend to make the Wassermann negative perhaps for this reason.

The most troublesome of all are the doubtful reactions. If it is supported by some clinical evidence or a history of syphilis, the doubtful test adds to the presumption of syphilis. If it lacks this support it but creates a suspicion of syphilis. An equivocal situation remains in either case. Beyond repeating the test there is little the serologist can do. In borderline cases repeated tests may clear up the uncertainty, the average being in favor of either a positive or negative. The effect of therapy, both on the clinical and serological

picture, may solve the difficulty. It is our practice in the Syphilis Department at Johns Hopkins Hospital to titrate these serums in larger quantity and note the effect of treatment. From our observations on these serums we feel convinced that there is a so-called provocative test. The doubtful test may clear up under treatment, or the test may become completely positive. In either case the interpretation is the same and a diagnosis of syphilis is entered. It has repeatedly happened in our experience that a Wassermann test which has become negative under a course of arsenobenzol compounds followed by a course of mercury may become doubtful or even positive after the administration of another dose of arsenobenzol. The reaction is usually of very brief duration.

Owing to the lack of space I have tried to confine this paper to the more practical considerations of the subjects and have eschewed many interesting theoretical discussions and much experimental data which would rightly belong in it.

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# THE PREPARATION OF THE COLLOIDAL GOLD SOLUTION

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IN view of the general recognition of the value of the colloidal gold test and of the difficulties so often encountered in the preparation of a suitable solution, we believe it worth while reporting a technic which we have found to be simple, rapid, and entirely dependable. Since a report upon this work with some theoretic discussion has been published elsewhere,\* we shall here present only a concise statement of technical details which may serve as a working guide to those interested in the subject.

## EQUIPMENT

The equipment required is as follows:

Distilling apparatus	500-c.c. beakers
Glassware:	10-c.c. pipettes graduated to .1 c.c.
1000-c.c. flasks	5-c.c. pipettes graduated to .1 c.c.
250-c.c. flasks	1-c.c. pipettes graduated to .1 c.c.
500-c.c. graduated cylinder	Stirring rod
100-c.c. graduated cylinder	One gross test tubes 12x120 mm.
1000-c.c. beakers	Test tube racks.

A three-gallon copper, tin-lined still gives very satisfactory service. For small quantities of distilled water, a still may be erected as follows: A section of block tin tubing four feet in length is bent near one end to form a wide arc. The short vertical section projects through a tight-fitting cork into a large glass flask. The long vertical section of tubing is surrounded by a glass condenser jacket twelve inches in length and passes through a loose-fitting cork into the receiving flask. This apparatus is supported on a ring stand by ring and clamp. A Bunsen burner with moderately high flame gives good and rapid distillation.

The flasks and beakers should be of resistance glass. Pyrex ware is quite satisfactory. The cylinders and pipettes should be of good qual-

\*Jour. Am. Med. Assn., lxix, 1855.



ity, but the calibration need not be of greater accuracy than that ordinarily employed. A thermometer may be used as a stirring rod, but, since accurate temperature readings are unnecessary, and the thermometer subject to breakage, a stirring rod is preferable. The test tubes need not be of resistance glass.

#### REAGENTS

Prepare the following reagents and solutions. They may all be kept as stock solutions.

Gold chloride	1%
Potassium carbonate	2%
{ Formalin	1
{ Water q. s. ad	40
{ Alizarin	1
{ Ethyl alcohol (50%)	100
Sodium chloride	1%
{ Potassium bichromate	200
{ Distilled water	1500
{ Add slowly	
{ Sulphuric Acid	500

Gold chloride may be obtained from Merek in one-gram quantities in sealed glass ampules. Baker's chemicals and Schering and Glatz' formaldehyde have been found satisfactory. Distilled water of the same quality as that used in the preparation of the gold solution should be used for the reagents. It is not necessary that the flasks in which the reagents are kept be of resistance glass. They should be carefully cleaned as outlined below and kept tightly corked when not in use. The same solutions may be used satisfactorily over many months. The bichromate-sulphuric acid solution is used in the preparation of the glassware and may be stored in an ordinary glass bottle and used repeatedly.

#### WATER

*Method of Distillation.*—The flame is turned high and the first distillate comes over rapidly, while no water flows through the condenser jacket, the steam cleaning the tube. After about 200 c.c. with the small apparatus, and 1000 c.c. with the larger, have come over, the flame is cut down until the water flows in discrete drops into the receiving flask. Distillation is stopped when approximately four-fifths of the contents of the distilling apparatus have come over.

*Number of Distillations.*—By carefully distilling as stated in the foregoing, a single distillation with this apparatus without preliminary treatment gives a water of sufficiently good quality to use with entire satisfaction. A singly distilled water from a Stokes still varies so widely at different times that it can not be depended upon.

*Storage of Water.*—Singly distilled water may be stored at room temperature in clean resistance glass flasks, if kept securely corked, for an indefinite period. The age of carefully distilled water has no influence on the character of the gold solution.

#### GLASSWARE

New glass should be secured and used for nothing else. The initial cleansing should consist of standing for thirty minutes in hot soap and water followed by a careful brushing under the tap; then hot dichromic acid solution for thirty minutes, followed by careful rinsing under the tap, then with distilled water. If this procedure is carried out as the initial cleansing, and the glass protected from dust and fumes while not in use, there need be no subsequent cleansing before use, save a brushing under the tap and rinsing with distilled water. The flasks should be tightly corked and capped with paper to protect from dust. The beakers should be wrapped in paper and the pipettes likewise. With this care, glassware may be kept in satisfactory condition with a minimum of labor.

#### PREPARATION OF COLLOIDAL SOLUTION

Using 100 c.c. as a basis for discussion, a beaker containing 100 c.c. of water is placed on wire gauze over a high flame. One c.c. of the 1 per cent gold chloride solution is added, followed by .8 c.c. of the 2 per cent potassium carbonate. Heating is rapid, and at boiling, 1 c.c. of 1 per cent formaldehyde is added. The solution should be vigorously stirred until reduction is complete.

It is not necessary to add the gold and alkali at any particular temperature. Our custom is to add them at once after placing the beaker over the flame. The formaldehyde, however, should not be added until the solution is boiling. If added at a lower temperature, vaporization of a considerable quantity of formaldehyde may occur, leaving an amount insufficient for complete reduction of the gold.

The amount of alkali used need not be exact, but should not go ap-

preciably below .7 c.c., or incomplete reduction will occur. As much as 1 c.c. may be used if at least 1 c.c. of formaldehyde is used (Lange's technic) and still give neutral solutions. The amount of formaldehyde used—within wide limits—seems to make little difference save in the rapidity of reduction. Since we have found that the chief cause of poor solutions—aside from the use of dirty glassware and water—is incomplete reduction, we have found it best to use a slightly greater amount of alkali than is theoretically necessary, and use a sufficiently large amount of formaldehyde to maintain a neutral solution. The slight excess of electrolyte does not change the curve in any respect.

The influence of the method of heating is decisive. Particular care should be used that the flame should not encircle the wire gauze and play upon the side of the beaker, as the irregular heating will produce an unsatisfactory solution. The stirring should be vigorous enough to equalize the temperature in all parts of the solution. If the formaldehyde is not added until boiling is reached, excessive vaporization of formaldehyde does not occur and can not be the cause of poor solutions. When large quantities are to be made, a multiple Bunsen should be used.

If a solution should be definitely alkaline to alizarin, it may be corrected by reheating to boiling and adding formaldehyde 1 c.c. at a time until the reaction becomes neutral. If the evaporation of water during the preparation of the solution is considerable, water may be added to restore the original volume. Solutions which are old and have become alkaline, but are still of good color and show no precipitate, may be made neutral by the use of formaldehyde and will give typical curves, whereas, before correction of reaction, the curve is materially altered.

#### ESSENTIALS OF A SATISFACTORY SOLUTION

Solutions should be transparent, orange or salmon red, and show no more than a slight shimmer by reflected light.

Five c.c. of the solution should be precipitated in one hour by 1.7 c.c. of a 1 per cent sodium chloride solution.

Slight alkalinity in a fresh solution does not alter the curve obtained.

Solutions satisfactory in color and not protected should show typical curves with abnormal fluids and no change with normal fluids.

Solutions which are alkaline after long standing or which show a blue cast or a precipitate are unsatisfactory for use.

## BRUCK'S NITRIC ACID TEST

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AS soon as the so-called Wassermann reaction was a firmly established and proven laboratory procedure of clinical significance, efforts were made to substitute a simpler test for syphilis.

The Wassermann demanding as it does special apparatus, care and training in its performance, to obtain dependable results is beyond the province of the average general practitioner. This fact makes the simpler test very desirable. The proof that results of the Wassermann do not depend on an antibody-antigen combination but on a substance that leans more toward the chemical than the immune mechanism justifies the presumption that a simpler chemical test may be possible.

Investigation has shown that in the blood (cells and serum) of some syphilitics certain reactions are present that are not present in normal serum. But all the tests proposed to take the place of the Wassermann have failed because of lack of specificity, or complicated tedious technic have rendered them unfit for practical clinical use.

The test under consideration was given to the profession by one of the originators of the Wassermann reaction. In fact the test first made practicable was done so by the combined efforts of Wassermann, Neisser, and Bruck.

A procedure recommended by a man of this standing and experience was bound to command attention and inspire confidence in the results reported.

Bruck found that the solubility of a coagulum produced by the action of nitric acid on blood serum varied under certain diseased conditions from that of normal serum. This was especially true of the coagulum of syphilitic serum. It was less soluble than that of normal serum.

Following his experimentation and investigation he proposed the following test: clear blood serum, free of red cells, is obtained in the usual manner, 0.5 c.c. of this diluted with 2 c.c. of distilled

water and to this is added 0.3 c.c. of nitric acid. Bruck worked with the German nitric acid which is about one-fourth of the strength of our American product. This acid should contain 24.77 gm. to the 100. gm. or 28.48 c.c. to the 100 c.c. with a specific gravity of 1.149. When added to the diluted serum, care should be taken not to allow the acid to run down the side of the tube, and slight agitation should be kept up as it is added so as to produce an evenly divided fine coagulum. This is allowed to stand at room temperature for ten minutes, then it is further diluted with 16 c.c. of distilled water and carefully shaken so as to insure thorough mixing without foaming; it is then allowed to stand for another ten minutes, when it is again carefully shaken (no foaming). The result should be noted in another half hour and at the end of twelve hours. If syphilitic, a distinct flocculent turbidity is present in the first half hour and in twelve hours a visible precipitate occupies the bottom of the tube, negative serum gives a clear or opalescent fluid with no precipitate.

Directions should be followed carefully and in detail. The amount of reagents used must be accurately measured, as it was these exact amounts that in normal serum proved soluble and in syphilitic insoluble. Glassware should be thoroughly cleaned, the water used must be free of all organic and mineral matter, and the time interval should be closely adhered to. In adding the nitric acid, it should be done with an accurately graded pipette that is used for nothing else, and dropped slowly but steadily into the diluted serum, care being taken that it was evenly distributed through the contents of the tube. The serum should be as fresh as possible and contain no red cells, although in my experience slight hemolysis did not seem to modify the end result.

In the cases reported every care was taken and in most instances a positive and negative control was carried along with the test, a serum that had proved negative being used as a negative control, and one having proved positive, as a positive. In any case in which the controls were not perfect the result was not recorded. In regard to serum showing hemolysis, I have taken on several occasions a specimen and after the clot had formed, removed a part of the serum. A test was made on the fresh serum and the result noted. The remainder with the other tube containing the clot with

TABLE I  
NONLUETIC CASES

CASE NO.	CLINICAL SYMPTOM	WASSERMANN	BRUCK NITRIC ACID
1	Eczema, palmar	-	-
2	Eczema, acute	-	+
3	Psoriasis	-	-
4	Eczema, chronic	-	-
5	Eczema, chronic	-	-
6	Influenza	-	-
7	Gonorrhea, acute	-	-
8	Gonorrhea, chronic	-	+
9	Eczema, chronic	-	+
10	Eczema, acute	-	-
11	Psoriasis	-	-
12	Influenza	-	+
13	Influenza	-	-
14	Influenza	-	-
15	Eczema, squamous	-	-
16	Gonorrhea, acute	-	-
17	Gonorrhea, chronic	-	-
18	Gonorrhea, chronic	-	-
19	Psoriasis	-	+
20	Influenza	-	-
21	Influenza	-	+
22	Gonorrhea, acute	-	-
23	Gonorrhea, chronic	-	-
24	Gonorrhea, complicated	-	+
25	Eczema, toes and feet	-	+
26	Influenza	-	-
27	Eczema, palmar	-	-
28	Eczema, arms	-	+
29	Gonorrhea, chronic	-	-
30	Influenza	-	-
31	Influenza	-	+
32	Eczema, acute	-	-
33	Eczema, general	-	-
34	Gonorrhea, chronic	-	-
35	Influenza	-	-
36	Eczema, facial	-	-
37	Eczema, infantile	-	-

\*Indicates variance with Wassermann. Wassermann negative in all cases. Bruck positive in ten.

serum was placed in the ice box until hemolysis was evident in the tube containing the clot. A test was again made on both the clear and the pink serum with controls, and the same results noted as obtained with the fresh serum.

Variation of twenty degrees Fahrenheit did not seem to modify results. The test is carried out at ordinary room temperature.

From a study of these tables it would seem that this test is to go the same way as the cobra venom, the mercuric chloride, the iodine

TABLE II  
KNOWN OR SUSPECTED LUETIC CASES

CASE NO.	CLINICAL EVIDENCE	WASSERMANN	BRUCK NITRIC TEST
38	Secondaries	+	+
39	"	+	+
40	"	+	+
41	"	+	-*
42	"	+	+
43	"	+	+
44	"	+	-*
45	"	+	+
46	"	+	-*
47	"	+	+
48	"	+	+
49	"	+	+
50	"	+	+
51	"	+	+
52	"	+	-*
53	"	+	+
54	"	+	+
55	"	+	+
56	"	+	+
57	"	+	+
58	"	+	-*
59	"	+	+
60	"	+	+
61	"	+	+
62	"	+	+
63	"	+	+
64	"	+	+
65	"	+	+
66	"	+	-*
67	"	+	+
68	"	+	+
69	"	+	-*
70	"	+	+
71	"	+	+
72	"	+	+
73	"	+	+
74	"	+	+
75	"	+	-*
76	Gumma (tibia)	+	+
77	" (pharynx)	+	-*
78	" (brain)	-	+
79	" (liver)	+	-*
80	Central nerve lesion	+	+
81	" " "	+	-*
82	" " "	+	+
83	" " "	-	+
84	" " "	+	-*
85	" " "	-	-
86	" " "	+	+
87	" " "	+	-*
88	" " "	+	+
89	" " "	+	-*

TABLE II—CONT'D  
KNOWN OR SUSPECTED LUETIC CASES

CASE NO.	CLINICAL EVIDENCE	WASSERMANN	BRUCK NITRIC TEST
90	Gave a history of lues with a chronic undefined condition presenting	-	-
91		+	-*
92		-	+
93		-	-
94		-	-
95		-	-
96		+	-*
97		-	+
98		-	+
99		+	-*
100		+	+

\*Indicates variance with Wassermann. At variance in twenty-two instances. Negative in seventeen cases where the Wassermann is positive, and positive in five cases where Wassermann is negative.

tests, and many others that have been suggested in the past. And still there is something about this test that impresses one who has studied and tried them all, and I firmly believe that every earnest worker who has worked with it feels that, perhaps, with some modification it would be a procedure of value.

As it stands today it is useless. It has neither a positive nor negative side that is dependable. Perhaps with a change in reagents, quantitatively, and the time interval, may give us a test that has a dependable side either positive or negative. In my investigation I have found the results in any given case to be constant even though at variance with the complement fixation. In cases 41, 58, 81, and 91 I have occasion to make several tests in each case and the Bruck result has been the same in every instance in each case.

If the test could be made dependable, it would be of great value in watching the effect of treatment on the blood picture, because of the ease of performance and the slight cost.



## A REVIEW OF THE ROENTGENOLOGY OF SYPHILIS

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OSLER,<sup>48</sup> in the 1917 edition of his textbook on the "Principles and Practice of Medicine," does not mention the use and application of the roentgen ray in the diagnosis of syphilitic lesions and manifestations, although in view of the accumulating literature on this absorbing topic a word from so high an authority would have been welcomed by the profession. That roentgenology is entitled to such consideration is shown, for instance, by the fact that Götzky,<sup>38</sup> at a meeting of the Southwest German and Lower Rhenish-Westphalian Society for Pediatrics, in 1913, presented a large number of roentgenograms showing syphilitic bone changes in children, in whom no clinical symptoms of the disease had been detected. Götzky emphasized the importance of the question whether such cases should be considered infectious and subjected to specific treatment.

The literature, although necessarily still of a comparatively recent date, deals with the congenital and acquired forms of syphilis affecting the human anatomy; it describes and illustrates the signs by which they can be detected, furnishes valuable pointers in the differential diagnosis between certain affections, and demonstrates the fact that roentgenology is not only valuable in supporting or refuting the clinical diagnosis but also in clinching it when ordinary methods of examination fail to be decisive.

Among the more recent contributions dealing with the general subject of roentgen diagnosis of luetic lesions is one by Blaine,<sup>7</sup> who states that syphilitic lesions which attack the osseous tissue occur in the hereditary and tertiary stages, and present the least difficulty to their demonstration. In soft tissues, he continues, the roentgen diagnosis is precarious. A gastric shadow defect with the stomach analysis pointing to ulcer, and with a positive Wassermann reaction, may be syphilitic, especially if antiluetic medication

shows a lessening of the defect, but postmortem work at the Cook County Hospital, Chicago, has rarely revealed syphilitic lesions of the stomach. As to the luetic involvement of other organs, there have been a few reports of roentgenologic evidence of pulmonary gumma, and the roentgen appearance of luetic aortitis is rather well substantiated.

#### SYPHILIS OF THE BONES

After describing the principal roentgen findings of syphilitic bone lesions, this author states that in syphilis of the periosteum the shadow may vary from a slight erosion to extensive raggedness, but it is difficult to distinguish roentgenologically between periosteal syphilis and simple inflammatory periostitis. The clinical history and the Wassermann reaction should always be taken into consideration. A subperiosteal gumma will distinctly lift the periosteum, while in luetic osteitis the bone cortex shows marked hypertrophy, resulting in raggedness and furring. Syphilitic joint lesions may show a considerable amount of destruction and involve the epiphyseal area. In conclusion, the author enumerates some differential roentgen points between syphilis and osteomyelitis, tuberculous osteitis, bone abscess, gout, sarcoma, carcinoma and osteitis deformans.

In this respect Brickner<sup>9</sup> commits himself to the following statement: "Next, of course, to the microscopic study of the tissue removed by incision, radiography supplies the most reliable differentiation between syphilis, osteomyelitis, sarcoma, carcinoma, cyst and tuberculosis of the bones." If this is intended to mean that histologic examination of removed living tissue is preferable to a roentgen examination to differentiate syphilis from carcinoma, it is a proposition to which no roentgenologist will agree. Every physician is aware of the fact that trauma is likely to stir up latent foci of carcinoma, producing widespread and dangerous metastases. The differentiation between syphilis and carcinoma should be made on other than microscopic grounds if this test involves the practice of biopsy.

In reviewing Brickner's article in detail which deals particularly with the roentgenographic diagnosis of syphilis, tuberculosis, tumors and osteomyelitis of the long bones, the subject of syphilis will be singled out for present purposes. He states that syphilis of

the bones is essentially an inflammation of the periosteum alone or of the periosteum and the bone itself. The most distinguishing features are thickening of the periosteum and of the bony tissue, especially the cortex, both of which produce black shadows. A light area is produced by gummatous destruction of the bone.

The periostitis may appear in scattered areas or along the entire length of the diaphysis, but the shadow is not always localized (as Brickner states), but may partake of quite a general character. Syphilitic periostitis begins next to the bone as a subperiosteal infiltration, so that the periosteal shadow, which in the early stages is usually narrow, is lifted away from the bone. In advanced conditions, as in localized periostitis gummosa, the shadow acquires considerable density, while a palpable periosteal gumma, being only inflammatory, causes no shadow.

Bone destruction due to gummata produces light areas surrounded by a dark shadow of reactive bone thickening, which differentiates this condition from osseous tumors and tuberculosis. When a gumma surrounds an island of bone, it appears in the roentgenogram as a sequester, but this is unusual in unmixed syphilitic osteomyelitis which also contrasts it with tuberculous and pyogenic osteomyelitis.

Brickner quotes Hochsinger as describing the roentgenographic features of osteochondritis of hereditary syphilis. They consist chiefly in thickening and periostitis with irregular absorption of bone at the epiphyseal end of the diaphysis, widening of the epiphyseal cartilage, the borders of which are jagged, and a calous shadow in the event of an epiphyseal separation.

As to the roentgenographic differentiation between (hereditary) syphilitic and tuberculous dactylitis, Brickner quotes Ware substantially as follows: Tuberculosis originates in the epiphysis, syphilis in the epiphyseal end of the diaphysis. In tuberculosis, periosteal thickening is absent or nearly so, in syphilis it is marked. Tuberculosis has a greater tendency to bone destruction, syphilis to bone production. Inflammation of the soft parts causes swelling in tuberculosis, while in syphilis this is largely due to thickening of the bone. Suppurating sinuses are often observed in tuberculosis, but only rarely in the syphilitic form. Multiple dactylitis may be syphilitic or rachitic but not tuberculous, as a rule.

Fraenkel<sup>31</sup> is convinced that not only tubular but also flat bones

with endochondral growth, such as the acetabulum and scapula, are subject to syphilitic ravages, having formed this opinion on his roentgenologic examinations of fetuses and infants, both living and dead. The majority of observations were made on the prepared and sawed bones and cadavers, while the examination of the living material was necessarily limited, because these patients usually perish at an early stage of their existence. The osteochondritic process in these bones is almost without exception associated with unilateral or bilateral ossifying periostitis, which is not necessarily proportioned in intensity to the degree of the osteochondritis. The flat bones are also involved in congenital syphilitic ossifying periostitis, the acetabulum particularly showing considerable osteophytic deposits. The ribs, likewise, were involved in all cases in which the tubular bones were affected, and, in view of the ready accessibility of the ribs to the eye, their examination would be the simplest means of obtaining information as to the presence of a syphilitic bone affection. Fraenkel considers it a direct law that there is no osteochondritis anywhere, unless the ribs participate in it. He is not equally positive in regard to periostitis ossificans congenita syphilitica. As to the osseocartilaginous border of the ribs, the anatomic and histologic examination is superior to the roentgenologic, although an inspection of the roentgen plate, especially of general surveys, furnishes valuable pointers from the condition of the rest of the skeleton.

In a later article, dealing with epiphyseal detachment and congenital syphilitic osteochondritis, Fraenkel<sup>30</sup> wishes to demonstrate the fallacy of the expression "epiphyseal detachment." Referring to the roentgenogram accompanying his article the author points out that on inspection of the upper extremities it may at once be seen that the separation at the proximal end of both humeri is some distance away from the upper end of the shaft of the humerus. At the distal ends of the bones of both upper arms there is ossifying periostitis which increases in degree at the ulnæ and is particularly pronounced externally.

In regard to the locality of the epiphyseal detachment, Fraenkel's observations differ considerably from those of Hochsinger. While the latter found the epiphysis of the distal humerus involved in six cases, Fraenkel has seen detachment of the epiphysis at that place

only once. At the lower extremities Hochsinger has never observed a displacement between epiphysis and diaphysis, while Fraenkel has seen this condition in two fetuses and in a seven weeks' old infant, using the roentgen ray as the method of examination. There can be no doubt, therefore, the author holds, that epiphyseal detachment at the lower extremities occurs also in living congenitally syphilitic children, although he admits that it predominates in the upper extremities.

Fraenkel emphatically contradicts Hochsinger's assertion that the osteochondritic process at the upper extremities develops most intensely and most frequently at the distal epiphysis of the humerus. This, he maintains, is at variance not only with the statement of Wegner, the discoverer of the disease in question, but also with the roentgenologic examinations of the skeletons of congenitally syphilitic children, made by Fraenkel himself. Indeed, Wegner states that the lower epiphysis of the humerus is constantly the least affected part, and Fraenkel has observed its involvement only in a single case. Similarly, Hochsinger's statements as to the epiphyseal detachment of the distal humerus end are directly contrary to the results of anatomicoroentgenologic examinations.

Fraenkel further disputes Hochsinger's contention that the absence of reactive manifestations in detachments, as seen in stillbirths, is a regular occurrence. In maintaining the exact opposite, Fraenkel refers to illustrations published by himself. Similarly Hochsinger's statement that epiphyseal detachment in stillbirths is often found in all tubular bones, whereas in infants several weeks old only one or a few epiphyses are detached, is, according to Fraenkel, contradicted by roentgenologic examinations in which rough handling is out of the question. The detachment occurs in different directions, oblique or transverse, but never at the borderline between diaphysis and epiphysis, as stated by Hochsinger.

Another point on which these two authors differ concerns the roentgenologic visibility of hereditosyphilitic epiphyseal detachment, which Hochsinger denies, while Fraenkel maintains that the roentgen method is simple, elegant and reliable, not only in regard to establishing the occurrence of the condition but also in following up of the curative process.

Fraenkel claims to have discovered the roentgenologic fact con-

sisting in the observation of the involution of osteochondritic manifestations under the influence of antisymphilitic therapy.

The bones in congenital syphilis also form the subject of an article by Post,<sup>50</sup> the object of which is to show by a number of roentgenograms that the pathologic processes observed by pathologists in the preroentgen era, may be confirmed by roentgen plates. This refers particularly to the line of ossification, spoken of as osteochondritis, which was first described by Wegner in 1870. The infantile changes due to pseudoparalysis or Parrot's disease are recognized quite early by the roentgen rays and allow of a diagnosis of syphilis in some cases of stillbirths without a necropsy. How long it is possible to trace the effects of this osteochondritis in older children, is not yet determined.

The thickening of the cortex of the long bones as a result of periostitis is well marked in a great many cases and of great value in the diagnosis of doubtful cases. There may also be periosteal changes as occur in the acquired form, as well as osteoperiostitis and gummata. Certain changes in the bone, analogous to osteomyelitis, are not always easy to recognize as due to syphilis and are often regarded as tuberculous or purulent infection.

Diefenbach's<sup>22a</sup> article on the roentgen ray diagnosis of diseases of bones is a general survey of the usefulness of roentgenology in the diagnosis of bone lesions. Insofar as syphilis as the causative factor is concerned, the author states that congenital syphilis, lues hereditaria lata and gumma, show characteristic shadows on the roentgenogram. In congenital syphilis there is periosteal enlargement about the metacarpal bones or phalanges, or the metatarsal or tarsal bones may be affected similarly. The periosteal shadow appears like a cloak hung about bone and this dark envelope is characteristic of congenital syphilis.

Symphilitic periostitis or gummatus periostitis presents the following points in roentgenologic diagnosis:

1. Irregular contour of periosteum.
2. When the continuity of the periosteum is destroyed, the tissue appears as if moth-eaten or reticulated.
3. Sclerosis of bone with increased shadow of the bone is always an accompaniment of syphilitic invasion.
4. In certain locations, as the anterior surface of the tibia, a

curve or bowl-like protrusion is formed, due to the bulging out of the periosteum.

Differentiating these diagnostic points from other bone lesions, the author mentions the characteristics of periostitis due to infection or trauma, nonsyphilitic osteomyelitis, peripheral sarcoma, and tuberculosis of the bone.

Cameron<sup>12</sup> reports the case of an infant, six weeks old, in which the roentgen rays showed increased thickness of the periosteal bone, the outlying masses of bone lying beyond the outline of the shaft, and the irregular shadow of the line separating the epiphysis from the diaphysis. He classifies this case as one of syphilitic epiphysitis of the lower end of the right femur and mentions the peculiar facts that there were no obvious clinical symptoms of the disease, that the patient's twin brother showed no clinical evidence of syphilis, but that both infants and the mother gave a positive Wassermann.

To the late Bela Alexander we are indebted for two communications<sup>1, 2</sup> on syphilis of the fetal spinal column. In his first communication he has shown that it is possible to visualize roentgenographically the finest details of syphilitic development in the fetal bones, and that some of these details are so fine as to be macroscopically indistinguishable. His studies have shown much that was new in the development of fetal bones and in fetal pathology generally.

In his second communication Alexander deals with the syphilitic changes in the ossifications of the *massae laterales* and sternum, at the same time discussing the development of syphilitic changes in the fetal diaphyseal ends.

The point the author makes in his first article is that syphilis does not interfere in any way with the regular occurrence of the osseous points—the incipient and further development of the ossifications. But when such development has progressed to a certain degree, where the inner structure commences to shape itself in the cartilage which is partly enclosed in the perichondral, periosteal ossification, the picture of enchondral bone fibers or trabeculae is distinctly traced by the roentgen rays, and with it the characteristic marks which indicate the syphilitic changes.

Since then he has followed the subject up by further studies and observations, coming to the conclusion that while syphilis does not

prevent the development of ossifications, its presence is manifested by characteristic pictures which undergo changes according to the course of development of the diaphyseal ends. As an example, Alexander selects the lower end of the developing femoral diaphysis, illustrating the minute radiation of the inner osseous fibers within the cortical cylinder which has become quite thin. There is, furthermore, the very light calcification zone, which is divided into two unequal layers by a dark line representing a very thin stratum of a softer substance more permeable to the roentgen ray. The narrower end zone corresponds to the calcification layer, with which normal ossification begins. It does not run in a straight line but is uniformly wavy or dentated. It can not always be distinguished with the naked eye in a bone specimen. The calcification layer above the end zone is attributable to syphilis and is due to the pathologic process.

In a similar way the author describes conditions of the lower femoral end, ulna and radius.

It is not the superficial interpretation of the general picture but of its integral parts that will lead to a correct understanding of the conditions, because each bone picture will appear different according to its size, diameter, position and distance from the plate.

In about sixty congenitally syphilitic children, with positive Wassermann, Duenzelmann and Schmitz<sup>25</sup> found that the roentgen rays demonstrate nearly always osteochondritic and periostitic bone affections of the extremities, even when no signs point to clinical changes of the bones. The authors strictly distinguish between epiphyseal, secondary periosteal and diaphyseal periostitis, the latter being an osseous affection independent of osteochondritis which always points to an advanced stage of syphilis.

The scabbard-shaped tibia, or Fournier's *tibia en lame de sabre*, is discussed in Professor Axhausen's<sup>9</sup> contributions to bone and joint syphilis. This unshapely thickening and arching of the tibia has been considered pathognomonic for hereditary syphilis. The fundamental change of the osseous structure is reflected in the roentgen findings which confirm the loss of division into a smooth compacta and a medullary cavity. Instead, there is a uniform, usually distended, diffuse, spongy bone shadow. Not infrequently remnants of the compacta in the course of transition may still be



recognized within the diffuse shadow, and in such cases the gradual disintegration and wasting of the old bone may be observed with considerable distinctness.

Recent roentgenologic observations tend to clear up to some extent the inner enormous structural changes—exostosis and enostosis—which occur in this affection.

Roentgenograms of diffuse bone syphilis greatly resemble those of transplanted tubular bones in the transition period. Aside from the deposits of periosteal and myelogenous newly formed spongy bone, it can usually be distinctly observed how the compact, transplanted bone is gradually absorbed by these newly formed masses. This process is perfectly cleared up. The transplanted bone becomes entirely necrotic, the surrounding organs which are still capable of ossification (the covering periosteum and parts of the medulla) remaining alive and active. Every necrosis exerts a stimulus on the surrounding material, which is capable of ossification, causing proliferation and formation of new bone tissue which encircles the dead bone, grows into it and forms a substitute mass. This process continues until all of the necrosed bone is replaced by live bone. Thus, the recognition of necrotic bone by the side of living ossifiable material must be considered the cause of the anatomic process and the explanation of the roentgen picture.

Codman<sup>17</sup> states that in the late forms of hereditary syphilis other bones are rarely found affected unless tibias are also affected. Extreme cases give a "saber-shaped" tibia, but when this condition is present, the fibula also shows localized areas of cortical thickening. There may be a "bone blister," due to localized gummatous formation under the periosteum. Occasionally there is localized destruction of bone substance on the diaphyseal line, but when this is so, there is also increase of the cortical bone in some portions of the shaft. Interference with epiphyseal growth may cause relative shortening of ulna and radius.

Fritzsche<sup>32</sup> deals with the same subject from a different angle. He describes a case of scabbard-shaped tibia as illustrating the fact that this anomaly may be the result of acquired syphilis in the adult provided external local irritation conduces to the production of favorable conditions. This happened in the case of a woman, 54 years of age, who had been infected by her husband but showed no

other clinical syphilitic signs but the tibial convexity. She had been in the habit of steadying herself against the edge of the bed when lifting her husband, and this caused a "blister" and subsequently a thickening of the tibia, which in the course of time assumed a bulging curvature. This was associated with severe paroxysmal pains in the leg and knee-joint which greatly interfered with walking. The Wassermann was positive.

The roentgenogram at once revealed a striking curvature, elongation and thickening of the tibia, forming an arch over the perfectly normal fibula. The osseous structure of the tibia was markedly changed. As a whole, there was pronounced condensation of the osseous substance, interrupted, however, by irregular transparent surfaces of elongated form and again surrounded by particularly dark shadows. At the edge there were irregular periosteal deposits, especially toward the upper region; distally the tibia merged into normal form and structure.

A case of late hereditary syphilis is reported by Badin<sup>4</sup> in a six-year-old girl, whose right knee was in pronounced valgum position. There were no pathologic manifestations up to the age of 13 months, when the right knee became swollen and the lower leg turned outward, without causing any pain either at rest or when walking. Since then a number of physicians instituted various treatments, all of which served to exaggerate the condition. The family history elicited nothing specific with the exception of a gonorrhea which the father contracted eleven years previously. The clinical examination of the patient revealed numerous other skeletal deformities and the roentgen examination furnished the following findings:

The upper and lower regions of the femoral diaphysis of the right leg were enlarged, deformed and pervaded by numerous foci of rarefying osteitis. The two condyles had a downward and inward direction; and the greater part of the epiphyseal cartilage seemed ossified. There were osteoperiostitic lesions of the tibia, and the articular surface was deflected downward and outward. Traces of rarefaction were also found on the upper part of the perineum. The upper part of the femur was swollen, especially toward the inner side, and deformed. The head of the femur was in complete anteversion, the neck in the coxa valga position. The entire osseous substance in this region was extremely rarefied. The iliac bone was

maldeveloped, serrated and thickened. The os pubis also showed rarefaction. The bones of the hands were similarly affected.

From these findings the author concludes that the genu valgum was merely a symptom of hereditary syphilitic ostitis, after excluding chronic osteomyelitis which would have been accompanied by fever, violent pain and abscess. Tuberculous ostitis would have involved the articulation long ago; the evolution and roentgenologic appearance of osteosarcoma are totally different; and osteosarthyrosis, osseous cysts and osteomalacia were similarly ruled out. When, moreover, the Wassermann test proved positive, the necessary treatment was instituted. Ten months later the reaction was negative and remained so, although the treatment was discontinued when this had effected a change as favorable as could be expected.

Pied<sup>49</sup> reports two cases of syphilitic Pott's disease principally for the reason that they have all the earmarks of syphilitic infection without showing any portal of entry of the virus in spite of the most diligent scrutiny. The final conclusion Pied feels himself constrained to formulate is that the original sore consisted in a chancre located deep in the urethra.

The first patient, a man 57 years of age, had previously been cured of facial paresis and lichen planus by specific treatment. These complaints have returned but as they do not cause any pain, the patient pays no attention to them. On the other hand, he has suffered for thirty years exceedingly painful neuralgic crises, the pain occurring in the body below the shoulders, very rarely in the arms and legs and never in the neck or head. The pains are worse at night and defy all medication.

Physical examination revealed two large curves from the fifth to the twelfth dorsal vertebræ, kyphosis and scoliosis, with the convexity to the right. Deep pressure there produced an anxious feeling. These and other clinical findings prompted a diagnosis of very slow curving of the spinal cord under the influence of syphilis. Antiluetic and orthopedic treatment was instituted with the result that the general condition of the patient improved considerably, while the curvature of the spine remained.

A colleague made the roentgenologic examination without having been informed of the suspected syphilis, the patient's transportation for that purpose having been previously impossible. The

roentgenogram confirmed the spinal lesion at the indicated place. The vertebral bodies were less dense than the others and showed differences in hue. The absence of intervertebral spaces was particularly striking. The entire mass of bone seemed to consist of one piece of nonhomogeneous density. There was neither gap nor displacement, but the region from the fifth to the ninth vertebra ran off at a certain angle from the vertebral column. These findings indicated the destructive and reconstructive nature of the lesions, which characterizes syphilis of the bones.

The second case concerns a young man of twenty-four, who had met with a painful accident to his spine during gymnastic exercises. After two years' treatment he was discharged, but the pains continued to a slight degree. As they increased, a slight deformity of the lumbar vertebræ appeared, for which he underwent orthopedic treatment. This failed to heal the lesions. A Wassermann test could not be made on account of the prolonged arsenical therapy. The family and personal histories were negative.

Two years after the accident the patient experienced persistent difficulty in micturition, but there was no pain. At all events, the diagnosis of syphilitic Pott's disease could be made only on the strength of the clinical and roentgenographic findings, and the patient was placed on cacodylate iodohydrargyric medication. After a few months he had so far improved that he could walk without difficulty or pain, and the spinal deformity was scarcely noticeable.

An interesting case of syphilitic spondylitis is reported by Ziesche,<sup>58</sup> in which roentgenography was instrumental in confirming the diagnosis already made clinically. In view of the fact that spondylitis may be due to trauma, infection, tuberculosis or syphilis, and that the treatment must be directed to the cause, a correct diagnosis is of the utmost importance. Roentgen examination was made in the lateral exposure on the day of admission. The first cervical vertebra is normal. There is a semicircular erosion, the size of a filbert, in the anterior wall of the epistropheus. Two dark lines, forming a T, probably due to firm bone margins in the distinctly visible osseous defect, seem to correspond to the sequester. The second and third cervical vertebræ are entirely displaced, disturbing the normal parallel position of the spinous processes and

the uniform interspaces between them. The impression is as if the greater part of the third vertebra were already sequestered, a narrow osseous bridge remaining as the only connection. From the fourth vertebra down the picture is normal again.

In the course of the antisyphilitic treatment a piece of bone was coughed up, after which the violent coughing ceased and the foetor ex ore decreased, with improvement in the condition of the patient. A second roentgenogram at this juncture shows considerable change. The defects seen in the first picture are considerably more pronounced. The atlas again is normal, but of the epistropheus only the upper part can be indistinctly seen. The body of the third vertebra is indistinct and thickened, especially the anterior part. By the expulsion of a large piece of the epistropheus the third cervical vertebræ have moved backward and this imparts a threatening spinous process having simultaneously descended. The two involved vertebræ have moved backward and this imparts a threatening aspect to the picture of the upper vertebral column. A very pronounced gibbosity has formed in place of the normal position. There is diastasis of the spinous processes which considerably diverge, while at the first examination they were still in a fairly normal direction. The most prominent point of the gibbosity is at the epistropheus, whose spinous process together with that of the third vertebra is thereby displaced backward and downward, causing subluxation and an approximation of the anterior vertebral surfaces toward each other. The impression is as if complete destruction of the second and third cervical vertebræ with subsequent compression of the spinal cord were immediately imminent.

A few days later the patient coughed up another piece of bone which appeared to belong to the third cervical vertebra. Further precautionary orthopedic measures were taken in view of the danger of a spinal compression.

From that day the course of healing took a favorable turn and after three months the supports were removed. The cicatrization was found to be complete and the head was freely movable without any particular complaint. A roentgen examination at this juncture revealed the following:

The position of the cervical vertebræ in relation to each other has again adjusted itself to normal, the previously distinctly visible

posterior displacement of the second and third vertebræ being no longer noticeable. The body of the epistropheus is distinctly smaller, and there is a round, bright place in its interior. It is uncertain whether this place corresponds to a connective tissue process of restitution or indicates a still existing fresh gummatous focus. The body of the third cervical vertebra is almost completely missing. The bright interstices which in normal roentgenograms indicate the intercerebral discs, are absent between the third and fourth vertebræ.

#### SYPHILIS OF THE JOINTS

On the subject of the syphilis of joints, Young<sup>57</sup> states that the most characteristic lesion to be noted is a thickening of the periosteum, due to successive layers of deposits at the juncture of the diaphysis and epiphysis. Unlike the blurring of the negative seen in early tuberculosis, the outlines of the bones entering into the formation of the articulation are distinct in outline. When characteristic osteitis is present, there is a darkening of the shadow from sclerosis of the bone above the area of activity within a thinning at the seat of active inflammation. A destructive area is quite distinct and never has the mottled, spotted, or grossly irregular appearance met with in malignancy.

An adult suffering from tuberculosis and syphilis of a joint will offer difficulties in the way of diagnosis, which will be simplified by the discovery of lesions in the diaphysis of the long bones due to an ancient periostitis, the thickened, striated appearance of the periosteum being almost pathognomonic of syphilis.

Brickner,<sup>9</sup> in his article previously referred to, writes with reference to syphilitic joints that, when the osseous tissues are clearly invaded, they produce the same type of shadows as in syphilis of the shaft, periosteal involvement and bone production. Gumma of the articular end of a bone is recognizable, while destruction of the articular surface by gummatous chondritis is less easily distinguished. Bilateral arthritis or synovitis points to syphilis rather than tuberculosis.

Ely,<sup>28</sup> in an article on diseases of joints and bone marrow, believes that syphilitic arthritis is often mistaken for other affections and proceeds to give a description of it. He mentions two well differentiated forms which correspond to the synovial and bony forms of

joint tuberculosis and probably to two others; the multiarticular variety and Charcot's joint.

The rarer form of joint syphilis is a synovitis which occurs in the tertiary stage, usually in the knee, without any tendency to involve the bone, unless as the result of unwise operative measures. The author shows the roentgenogram of the knee joint of a child after treatment for two years with a diagnosis of tuberculosis. The illustration shows the diseased tibial epiphysis and the proliferating osteitis of the femoral shaft at about 4 inches above the joint. A second roentgenogram shows the improvement in the tibial epiphysis and the gouged-out appearance in the femoral epiphysis four months later, after two injections of salvarsan and a course of mercurial inunctions.

A more severe and more frequent form of syphilis occurs as a proliferating inflammation of the marrow and inner layer of the periosteum, with or without an inflammation of the synovial membrane. Not only are the clinical pictures of this affection and joint tuberculosis often the same, but an expert roentgenologist may not be able to distinguish between them, so that other signs of syphilis must be depended on for a differentiation.

The multiarticular form occurs almost certainly as a late syphilitic manifestation. Several roentgenograms illustrate this form by the swelling and flexion of the fingers, the superextensions of the phalanges, the rarefactions and destruction of the bone ends, and the bony ankylosis. In one case the wrist bones and the radii were involved, and in another all the interphalangeal joints with bony outgrowths.

#### CHARCOT'S JOINTS

In the diagnosis of Charcot's joint Ely does not mention the use of the roentgen ray. Further information on this subject can be gleaned from Case's<sup>16</sup> article on the roentgenology of chronic joint diseases. According to this author, roentgen ray findings in early syphilitic involvement of the joints are not characteristic. Unless there develops a synovial effusion or unless evidences of characteristic osteoperiostitis are discovered, the findings are not likely to be different from those of acute articular rheumatism.

Ely quotes Redard as mentioning the following diagnostic characteristics: Clear blotches at the level of the epiphysis, indicating

the presence of an interosseous gumma and the evidence of a rarefying osteitis, the increase in the circumference of the bones seen especially in the epiphyseal region, the osteophytes, the irregularity of certain portions of the bones, and spontaneous fractures.

The roentgenogram does not record the exact size of gummatous deposits which are not ossified, since new-formed bone is still permeable to the roentgen ray. The ossifying process involving the capsule gives rise to a varying quantity of osseous debris within the joints, well shown in roentgenograms of typical cases.

From the x-ray standpoint the typical findings in tabetic arthropathy are the extensive proliferating and destructive processes which run a parallel course and lead to extracapsular ossifications due to bone formation in the fibrous layer of the joint capsule. Fluid in the joints, subluxations and pathologic fractures, and often the absence of pain on motion are other diagnostic features of importance. The bone lesion sometimes resembles sarcoma.

In a Charcot ankle there is likely to be an inversion of the foot, owing to the absorption of the lower end of the tibia and possibly also of the astragalus. In contradistinction, Pott's fracture is always an eversion fracture.

In incipient cases differential diagnosis is difficult. The absence of pain is a constant finding in these cases, yet in some instances the movements of the joints are exceedingly painful.

In the tabetic form of syringomyelia, arthropathy occurs in about 10 per cent of the cases. Thickening of the bones in the region of the epiphysis, osseous layers which are poor in calcium salts, an atrophic condition of the bones, and occasional joint symptoms sometimes appear on account of interference with the trophic impulses.

According to Blaine,<sup>7</sup> Charcot's joint has a rather characteristic roentgen appearance. The changes vary from a slight irregularity of outline which may be difficult to distinguish from an early arthritis, to an enormous joint destruction in which all resemblance to the normal joint has been lost.

According to Young,<sup>57</sup> Charcot's joint is characterized by destructive atrophic changes in the epiphysis from friction, which are mechanical in character. The symptoms of tabes dorsalis are so characteristic and the syndrome so easily recognized, that the diagnosis



of this condition is quite apparent to the intelligent diagnostician.

Matsuoka<sup>42</sup> contributes an extensive article on the subject of articular affections in tabes dorsalis. He reports the case of a 53-year-old alcoholic who admitted previous syphilitic and gonorrheal infections:

*Roentgen Examination.*—Ventrodorsal exposure of the right hip joint in the median position. The fracture line is in the lateral section of the femoral neck near the trochanters, indicating a lateral fracture of the neck. The lower fragment is considerably displaced upward. There is no impaction of the two fractured bone ends.

*Tibiofibular Exposure of Both Knee Joints.*—The articular cavity of the left knee casts a very hazy shadow, in which no bone changes can be recognized. Two sesamoid bones are present in the posterior part of the left knee, but not in the right."

Another case described by this author concerned an arthropathia tabidorum of the right knee in a 52-year-old workman, whose father had died of an affection of the spinal cord and senile marasmus. The patient had syphilis at the age of 30 years. Three years ago his eyesight became affected, followed by articular rheumatism and severe pain in the right knee joint, which became loose and swollen without any inflammatory manifestations.

*Roentgen Examination.*—Tibiofibular exposure: In the diaphyseal part of the femur considerable newly formed bony tissue can be palpated on the anterior surface of the femur which gradually disappears toward the knee joint. Cloudy shadows are cast from tissue impervious to the rays in the articular cavity. The patella gives a thin shadow. The curvature of the articular surface seems to be somewhat diminished. The proximal part of the femur casts a thin shadow. The articular line is not visible. The tibia and fibula are close to the articular surface of the femur. The articular surface of the tibia is not visible. The proximal end, as well as its epiphysis are irregularly thickened, casting a deep shadow. The tibial tuberosity is slightly prominent anteriorly. The tibiofibular articular line is blurred. The proximal part of the fibula is distinctly thickened. At the place corresponding to the patellar ligament a deep shadow can be recognized, but it is difficult to

decide whether or not this structure is an ossified mass in the patellar ligament.

*Ventrodorsal Exposure of the Right Knee.*—Both bones of the lower leg are distinctly displaced outward. Within the joint there is a free piece of the bone of the tibia which is distinctly separated from its proximal end by a light zone. The opposite part of the tibia shows an oblique smooth surface; the proximal tibial end shows a fanlike widening upward. At the inner side free blurred shadows can be recognized. The head of the fibula is fractured and distinctly separated from the proximal end of the fibula by a light zone. This separated part of the head of the fibula is firmly adherent to the external part of the tibial epiphysis. The medullary cavity of both bones is only faintly discernible.

This, then, was a case of epiphyseal fracture of both tibia and fibula with irregular thickening of the proximal parts of these bones.

In connection with these cases it is of interest to note that long continued antisypilitic treatment remained unsuccessful.

The third case was that of a well-nourished man of 43 with arthropathia tabidorum of the right knee. The history contains no mention of syphilitic infection, and antisypilitic treatment was unsuccessful.

*Roentgen Examination.*—Ventrodorsal exposure of the right knee. The middle femoral condyle is enlarged in the form of a club. The lateral femoral condyle is partly ground off, casting a deep shadow. The patella is distinctly visible. The intercondyloid eminence can hardly be distinguished. The head of the fibula is close to the tibia. The articular cavity is more or less blurred.

In discussing the theories of arthropathia tabidorum of Buzzard, Senator, and Rotter, Matsuoka finds that none of them apply to his three cases. On the other hand, he approvingly quotes Pitres and Vaillard (after Blenke), who found degeneration of peripheral nerves in a tabetic cadaver and hold that arthropathia tabica is caused by trophoneurotic disturbances. These observations were soon afterward confirmed by Oppenheim and Siemerlin in a large number of autopsies.

Matsuoka concludes that it is probable that the nerves supplying the joints participate in such a process of degeneration, leading to a secondary infection of the joints. He thinks it probable that

osteoarthropathia tabica is caused by the affection of the nervous system.

#### TABETIC AFFECTIONS

Krüger<sup>37</sup> likewise contributes a detailed article on the subject of tabetic arthropathy. He thinks that, although the diagnosis in advanced cases is not difficult with the aid of a roentgen examination, there are certain incipient articular affections that are difficult to differentiate. While the old mechanical explanation of arthropathy still holds good today for the progressive development of the disease, the original causative factors may include, (1) injuries causing bone fragments to scatter in the joint, and (2) gummatous processes or luetic periostitis.

The author reports several cases in which the roentgen ray was instrumental in determining the etiologic factor.

In a female patient, who was under treatment for a maxillary affection, a painless swelling of the left knee was accidentally discovered. Further clinical examination justified the diagnosis of *tabes dorsalis*, and the roentgenogram revealed incipient arthropathy. At the median articular surface of the tibia there were destructions which had the appearance of ulcers and at the outer edge proliferating processes could be recognized. Antisyphilitic treatment, puncture and finally amputation failed to save the patient's life.

Another case was that of a 51-year-old, powerful man, who had contracted syphilis thirty years previously and had gone through two inunction treatments. On admission, the left leg was diffusely edematous, with a distinct effusion in the left knee joint. There was pronounced lateral mobility of the lower leg. The Nonne reaction of the cerebrospinal fluid was positive, the Wassermann reaction of the blood was negative. The roentgenogram showed distinct destructions of the tibial articular surface, which had the appearance of ulcers, and there were proliferating bone processes of slight extent. The patient was still under treatment at the time of the report.

A third case, in which the rapid progress of destructive arthropathia tabica could be distinctly followed for about three years, was the following:

The patient was a laboring man, 46 years of age, who presented many clinical signs of tabes. The roentgenogram showed distinct destructions at the epicondylus medialis femoris and condylus medialis tibiæ, which had the appearance of indentations. Periarticular ossifications were already distinctly visible. The other knee joint was healthy. A later roentgenogram illustrates the progressive development of the destructive and proliferating processes in spite of treatment. One year after the first roentgenogram was made, the destruction of the articular surfaces had enormously progressed. The epicondylus lateralis femoris was almost completely eaten away, and the epicondylus medialis tibiæ was clumsily distended. Aside from the bony proliferations there was a denser shadow which might point to an agglomeration of an organic osseous substance. The fibula is displaced away from the tibia by interposition of bony proliferations in the connective tissue. The periarticular bony proliferations extend far in the proximal and distal directions; they almost creep upward along the femoral shaft.

There are also cases of arthropathy which commence with a slight atypical articular fracture. This happened in a healthy man of 37 years, who had slipped on a banana peel, sliding with the left leg forward and kinking in the right knee, without falling down. The knee joint was swollen without effusion. There was pronounced lateral mobility and distinct crepitation below the knee joint. The roentgenogram showed a small scattering of bone. After two months' treatment the patient was discharged free from complaints. Seven months later considerable effusion had taken place in the knee joint, and a roentgen examination disclosed a very rapid progress of tabetic arthropathy. The classic signs of tabes were not yet present, but the diagnosis was made on the strength of the roentgenogram and the positive reaction of the Nonne test of the lumbar fluid.

Another case of tabetic joint affection without classic symptoms, in a woman, 50 years of age, was observed by Professor Koenig, according to Krüger's paper. The roentgenogram showed advanced tabetic arthropathy, periarticular ossifications and destructions at the condylus internus femoris.

The author's experience goes to show that extensive proliferating and destructive processes, running an almost simultaneous course

and leading to considerable extracapsular ossifications, are typical roentgenographic signs. While the fact that the process may commence with an osseous lesion is not yet generally known, this can often be distinctly seen in the roentgenogram. There are cases of tabetic arthropathy in which no clinical signs of the general affection are at first apparent, but become evident at a later stage. In these cases of incipient tabes the joint evidence of the roentgen rays and positive Nonne reaction is of particular importance.

Carman<sup>13</sup> in 1911 summarized the opinions and reports on tabetic osteoarthropathies of ninety-six previous writers. Bibliographic references were attached. He also reported eight cases from his own practice, illustrated by ten roentgenograms. In all of these the roentgen ray gave information of value either by determining or confirming the diagnosis, or by contributing details. In no case did the joint trouble antedate other tabetic phenomena. In all cases but one the lesions were well advanced, and in that one the pathologic changes were shown in the wrists at an early stage of the disease. The marked roentgenologic features of Charcot's joint were summarized as follows: (1) Atrophy of the articular cartilages, (2) irregular destruction of bone, often associated in the same joint with (3) irregular hyperplasia of bone, (4) detached bone masses and detritus, and (5) translucent areas. He concludes as follows:

"1. With rare exceptions tabetic osteoarthropathies may be diagnosed by roentgenography alone.

"2. Only by the rays may detailed information be obtained as to the extent of involvement in tabetic joints.

"3. The roentgen rays will show joint lesions in tabetics, when ordinary clinical examination will not.

"4. The joints of all tabetics should be roentgenographed in the interest of the patient and in order that the earliest signs and manner of onset may be further elucidated.

"5. All joint lesions, except the very few in which the diagnosis is beyond doubt, should be examined with the roentgen ray."

Bering,<sup>6</sup> in a paper on articular affections in acquired syphilis, states that certain affections of this kind can not be referred either to early or late syphilis. In all probability articular syphilis has its primary seat in the articular capsule, but the diagnosis is not

always easy. If it can be made early, the prognosis is favorable. Untreated cases will end in grave articular disturbances.

In his clinical experience the author has applied roentgenology with a view to facilitating the diagnosis, but he succeeded only in a few cases in demonstrating a slight separation of bones into fibers. Only in one of the cases had there been any extensive bone changes, and there was absolutely nothing characteristic of syphilis in any of the plates.

The peculiar fragility of bones in syphilis and their reaction to traumatism are matters of common knowledge, and it is not surprising, therefore, that cases of unsuspected latent or congenital syphilis should be discovered by a roentgen examination of the bones, while examining the seat of fractures. In this connection, Coues,<sup>18</sup> in a paper on syphilis and trauma, states that our present increased knowledge of the importance of roentgenograms of the skeletal system makes the detection of latent syphilis, which years ago would have been unrecognized, a comparatively simple procedure.

Coues cites the case of an 11-year-old girl who was seen at the Surgical Clinic of the Boston Dispensary in 1912. In the careful examination for a fracture of the right clavicle which failed to heal, no signs of congenital syphilis were found, but a roentgenogram showed marked periostitis of the tibiæ. Under specific treatment union took place and the patient recovered rapidly. On another case, a diagnosis of sprained ankle had been made in a New York hospital in 1916, while the roentgen examination made by the author not only showed a subperiosteal fracture of the upper third of the left fibula, but also marked periosteal thickening and enlargement of the entire fibula and some osteoperiostitis of the tibia. Although the Wassermann test was negative, a history of syphilis was admitted, and under antisypilitic treatment the patient was able to walk again with a minimum amount of discomfort.

Another negative Wassermann case, reported by the same author, was that of a boy, 13 years of age, who was seen at the Boston Dispensary in 1913, for considerable pain and disability of the right elbow, following two falls striking on the same arm. Two small pieces of bone were removed, but no healing of the wound occurred. The Wassermann test was negative and a roentgenogram showed

the lower epiphysis of the humerus to be normal. But as the tibiae were tender to pressure, a roentgenogram of these bones was made which revealed a slight, though definite periostitis. Local and general specific treatment was instituted, followed by sudden great improvement, the elbow returning to normal in a short time.

A somewhat similar case was observed by the same author in a young married woman, a probable tabetic, who sought help for a swollen ankle due to a fall. While examination showed a peculiar soft, doughy and diffused swelling, unlike the ordinary swelling after fractures, it required the aid of a roentgenogram to disclose a fracture of the base of the fifth metatarsal bone. The mentality of this patient was affected and a history could not be obtained, but the case was evidently one of a painless fracture in a probable tabetic, which it required a roentgenogram to diagnose.

Meriel<sup>43</sup> reports the following case from the Hotel Dieu, Paris, at the early period of 1899. An insignificant fall caused a fracture of the upper end of the humerus in a 32-year-old porter, and roentgenograms revealed great rarefaction about the upper epiphyseal line of the humerus. It showed a juxtaepiphyseal fracture as well as an old fracture of the neck which had healed. The latest fracture was probably caused by muscular contraction with a rarefying specific ostitis of congenital origin, as the patient denied acquired syphilis. It is of interest that roentgenograms of an old fracture of the right humerus showed the same condition.

Coues<sup>15</sup> calls attention to the fact that a roentgen examination may indirectly lead to the discovery of unsuspected syphilis, when only soft parts have been injured and their resistance to treatment suggests the aid of the roentgen ray in the search for a possible fracture. This is exemplified by the following case:

A seemingly healthy chauffeur was seen in 1913 after an accident in which he was wedged in between a wall and a boulder. There were great pain, disability and ecchymosis of the right leg. Roentgen examination showed no fracture but extensive periostitis of the tibia and fibula of the injured leg. Facts suggestive of congenital syphilis were then ascertained, and when intensive specific treatment was instituted, there was immediate diminution of the swelling and pain, and the condition, which would have been unrecognized without the aid of the roentgen ray, was rapidly cured.

## SYPHILIS OF THE AORTA

The methods employed for the demonstration of syphilitic aortic dilatation are inspection, palpation, percussion, and the roentgen method, and Kraus,<sup>36</sup> in an article on the Heller-Doehle form of aortitis, shows that in the majority of cases there are roentgenologic signs which confirm the findings of the other clinical methods. Although the latter are generally sufficient to make a diagnosis, he advises resorting to roentgen control, whenever possible.

Syphilitic affections of the aorta also form the subject of a paper by Deneke,<sup>21</sup> who discusses the role syphilis plays in the etiology. After enumerating in detail the clinical methods of establishing a diagnosis of aneurysm of the aorta, Deneke states that in all cases of difficulty a roentgen examination far exceeds in value all diagnostic methods, adding that through that examination about one-half of all cases of aneurysm are detected. With the use of the two oblique diameters a really plastic picture of the aneurysmal sac can often be obtained on the screen. Only two sections of the aorta are not roentgenoscopically visible; one of these is the root of the aorta which is located within the heart shadow, and the other is the concavity of the arch in which only gross changes in the second oblique diameter may be recognized.

Eisler and Kreuzfuchs<sup>27</sup> have a great deal to say on the roentgen diagnosis of syphilis of the aorta. Aside from a diffuse dilatation of the aorta, a characteristic sign in the roentgen examination of aortic syphilis is that a certain part distinctly bulges more prominently than the rest, and on comparing the roentgenograms of aortic syphilis with those of aneurysms, it will be found that the difference is only one of degree and not of principle. This is in full agreement with the experience of pathologic anatomists and the authors consider Kaufmann correct in stating that on inspection of the typical pictures of syphilitic aortitis one is impressed with the idea that from this picture to that of aneurysm is only a small step. A large collection of roentgenograms of aneurysms and syphilitic aortitis in the Roentgen Institute of the Vienna General Polyclinic enabled the authors to recognize for each type of aneurysm a perfectly analogous type of syphilitic aortitis. They observed a diminished frequency of aortic syphilis of the ascending arch, and descending types in the



order named, and proceed to describe their observations as follows:

*The Ascending Type.*—The section which bulges more prominently than the rest of the dilated ascending aorta has the following characteristics: The ascending aorta which normally and under strictly symmetrical conditions runs within the vertical line drawn from the most prominent point of the right auricle, approaches this vertical line or transgresses it to a considerable extent. Simultaneously, however, the auriculo-aortic angle which is generally found at the level of the costal cartilage of the third rib, advances toward the diaphragm, so that a larger or smaller part of the aorta overshadows the right auricle. This is to be taken as a proof for the beginning of the process at the root of the aorta. This, again, is in complete agreement with the statements of pathologic anatomists. In good roentgenograms the shadow of the dilated aorta ascendens distinctly contrasts with the auricular shadow which it covers, because it is due to a substratum which is denser and closer to the plate.

The ascending type of aortic syphilis is the most frequent form, and its clinical diagnosis may meet with considerable difficulty in the absence of pronounced subjective symptoms, unless there is simultaneous aortic insufficiency.

*The Arch Type (Club-shape.)*—The dilatation commences where the ascending aorta fuses with the arch, resulting in a club shape even in the frontal aspect. When the bulging is more prominent either to the right or to the left, the club shape can still be recognized but has lost much of its distinctness. The symmetrical dilatation is evidenced in those cases in which the circumscribed bulging comprises the transverse part of the arch. Roentgenologically, it may be easily underestimated, although it presents pronounced clinical symptoms at an early stage, such as compression of the esophagus and trachea, with simultaneous displacement of the latter to the right, and jugular pulsation.

The descending type is characterized by a rather transparent shadow in the anterior aspect, running from the aortic arch either vertically down or with a lateral convexity toward the diaphragm. This shadow bridges over the angle formed between the aortic arch and the left ventricle. Although arteriosclerosis may also be an etiologic factor, the authors have seen cases with positive Wassermann reaction, but this type is the rarest of the three.

In conclusion, the authors mention the occurrence of cases of aortic syphilis with diffuse dilatation of the aorta, in which the roentgenograms fail to record any specific characteristics.

Lippmann and Quiring<sup>40</sup> deal with the roentgen examination of aortic affections, giving special consideration to syphilis of the aorta. They describe the technic of visualizing the aorta in general, and in the second part they describe the result of their examinations of luetic changes of the aorta as carried on with the technic previously described. They consider it important to strictly adhere to the details of the technic in all cases for purposes of comparison.

The authors found, in the first place, that fluoroscopy is not sufficient to determine initial aortic changes with the necessary distinctness, and the only method they have found applicable in all cases consists in distant instantaneous roentgenography at focus-plate distance of 1.5 meter, taken in the first oblique diameter. This will enable the roentgenologist to obtain a separate picture of the ascending and descending aorta and of the aortic arch practically in natural size, and the lumen of the ascending aorta thus obtained is measurable. It is not an easy matter, however, to maintain this exact distance, when the patient is turned, even when the distance between the chair and the plate remains unchanged. To overcome this difficulty, the authors fixed the posterior edge of the chair at a distance of 1 meter from the roentgen box, and if the patient was then rotated by the fluoroscopically determined angle into the desired diameter, the plate distance was about equal to that required for distant exposure. Even if this method does not yield results as exact as those obtained in orthodiography, they are so near the actual facts that they can be safely used for accurate comparisons.

Turning to the findings of the luetic aorta in particular, 160 cases were examined in the course of eight years. The material points were the following: The classic age of patients with aortic syphilis is 45 years. In 22 of the patients the aorta measured 3.5 cm. or more in width; in 4 more than 3 cm., and in only one (younger) man was it less than 3 cm. These figures considerably exceed those found in normal aortas. Furthermore, the intensity of the shadow of the aorta was greater, and in most cases far more intense than that of the ribs.

Comparing the results of fluoroscopy with those of roentgenography, it was found that in 107 examined cases, 97 showed a deeper aortic shadow and 100 a greater lumen. This again confirms the fact that greater width and deeper shadow are a typical sign for aortic syphilis. It should be noted, however, that in fluoroscopy the width could not always be determined and frequently led to mistaken diagnosis. In most cases the aorta is erroneously assumed to be narrower than it is, and even aneurysms have been overlooked in some cases. The bulging of the pulmonary artery is particularly difficult to visualize and is consequently rarely diagnosed correctly. The shadow density, however, can be roentgenoscopically well determined by the possibility of comparing it with that of the ribs.

The causes leading to the greater density of the aortic shadow can not be determined roentgenologically. It is theoretically assumed that it is caused by the increased lumen and the necessarily increased diameter of the blood column. But while in fifteen necropsies the authors found such to be the case, they also found in a number of other cases a massy thickening of the first part of the aortic wall, consisting of callosities as thick as the finger. At any rate, these callosities produce the same roentgen picture as an aorta with an increased lumen.

In comparing the roentgen plates with the results found at necropsy, the authors were also careful to observe whether or not the aortic sounds could be explained by an extension of the lumen immediately over the valve, as was to be theoretically expected (relative aortic insufficiency). But from the mere measurement of the plate results this idea proved untenable, because in the cases with aortic sounds the aortic diameter at the heart was narrower than higher up, so that the sound could not very well originate immediately above the valve. In these necropsies it was nearly always seen that the valve was impaired (with cicatricial contraction or drawn into the aortic scars), so that the sounds could always be explained by actual valvular changes.

The most valuable results in these examinations were furnished by some early cases without any aortic sounds whatever, and with positive Wassermann reaction. In these cases there was distinct widening and darkening of the aorta, and it was from these symptoms alone that it was possible to make an early diagnosis of the

condition and the consequent timely institution of the correct therapy.

Among the author's 160 cases, twenty-nine aneurysms were found in the presence of diffuse distention of the aorta. In two of these patients a roentgen diagnosis of bronchial tumor and mediastinal tumor, respectively, had been made, but the postmortems disclosed large aneurysms, one of which had compressed a bronchus. The valves were intact. The differential diagnosis between tumor and aneurysm often meets with a number of difficulties. The walls in aneurysms being usually considerably thickened and their cavities filled with thrombi, pulsation can not ordinarily be demonstrated, and the clinical findings of the heart are frequently negative when the seat of the aneurysm is high, with the consequence that the true facts are only revealed at necropsy.

From the author's experience, syphilis is one of the most frequent, if not the most frequent, affection of the aorta, and the physician should therefore always think of syphilis on finding the least irregularity in the aorta.

According to a report by Lieck,<sup>39</sup> the roentgenogram of a young man suspected of incipient tuberculosis presented the following peculiar features: Pulmonary fields normal. Two lentil-sized glands at the right hilus at the level of the seventh posterior rib. Heart shadow normal. Descending aorta uniformly distended up to 8 cm. The aortic shadow exceeded the spinal column by 2.5 cm. to the right and 2 cm. to the left. The aortic arch participates in this uniform distention. Furthermore, the aortic shadow is elongated up to the jugulum. The intensity of the aortic shadow was very slight and transparent to the details of the spinal column.

This suggested syphilis, which was admitted, but supposedly cured. After a rigorous salvarsan and rest cure, another roentgen examination four and a half months later showed that the aortic shadow was no longer uniformly dilated but had irregular contours, among which a distinct bulging to the right suggested an incipient aneurysm. The aortic shadow had also become darker.

Lieck raises the question whether an aortic change of the above description may lead to aneurysm and whether specific treatment may effect an improvement or at least arrest.

Syphilitic aneurysm of the left upper division of the pulmonary

artery is discussed by Warthin,<sup>54</sup> who presented a case with a definite history of chancre and skin rashes, with Wassermann four positive, showing at necropsy syphilitic lesions in the heart, aorta, liver, pancreas, adrenals and testes; furthermore, atherosclerosis and aneurysm of the pulmonary artery, in the walls of which *Spirochetes pallida* were demonstrated. Syphilis of the pulmonary artery and syphilitic aneurysm of the pulmonary artery are, therefore, for the first time conclusively demonstrated as pathologic entities.

A roentgenogram of the chest was also taken. The shadow of the aneurysm appears as a mass, somewhat larger than a hen's egg, on the left extending from the second to the fourth ribs, fairly well descended on its outer border, but less well defined elsewhere. The density of the lung shadow on both sides is great, but more marked on the left below the level of the second rib.

The report of the roentgenologist adds that these shadows do not have the characteristics of tuberculosis or of ordinary inflammatory infiltrations; that the exact underlying pathology is not discovered but is suggestive of neoplasm.

#### SYPHILIS OF THE LUNGS

A roentgenologic contribution to syphilis of the lungs has been published by Kayser.<sup>55</sup> It consists in the description of a case of hereditary gummatous syphilis of the lung which, aside from its rarity, is interesting because the author believes himself to have been the first to demonstrate roentgenologically the involution of gummatous syphilitic lung changes. The case is also of interest on account of its occurrence at the relatively late age of 12 years.

The clinical symptoms, the family and personal history, and the positive Wassermann reaction combined in making a diagnosis of syphilis of the lung, but before antisiphilitic therapy was instituted, it was decided to make a roentgenogram, which was followed by another two weeks later and a third at the end of the specific treatment, the intention being to verify the expected successful treatment and to furnish an object lesson for future comparisons.

The first roentgenogram shows a considerable infiltration of the entire right middle lobe with intense consolidations extending to the upper lobe. Nothing pointed to tuberculosis. The second roentgenogram was made two weeks later after inunctions with 30 gm.

Hg had been applied. A distinct involution of the entire process was apparent, the originally dense shadows having cleared up and the process in the upper lobe especially having receded. The clinical picture underwent a corresponding improvement.

The third roentgenogram was made four weeks after the second, the specific treatment having been discontinued in the meantime. The improvement of the condition was quite evident. The upper lobe was almost entirely free and there were no noteworthy remnants of consolidation in the middle lobe, with the exception of a few fibrous cords in the hilus region. The clinical improvement corresponded with the roentgen findings. It was clear from both the clinical and roentgenologic findings that the case was one of gummatous syphilis of the lung. If it had been of fibrous form, the process would have been incapable of clinical involution and, similarly, it would have been impossible for the roentgen method to record any involution of the original process.

A report on two cases of syphilis of the lung comes from Bauch.<sup>5</sup> In the case of a 51-year-old bachelor the diagnosis lay between tuberculosis and syphilis of the lung. Fluoroscopic examination showed marked dense bands of fibrous tissue over the entire right side. The left side was clear. The hilus glands were enlarged on both sides, and there were cavities and adhesions in the upper half. There was pneumothorax in the axillary position of the upper half. The lower half showed a dense, peribronchial infiltration, with marked density at the axillary portion of the base and with numerous enlarged bronchi. The quiet, evenly dense shadow at the lower axilla might be due to thickened pleura. The left lung is normal, except for the enlarged hilus gland. The mediastinum is displaced to the right. The right diaphragm is elevated and irregular. The ascending aorta is markedly widened. The heart is exceedingly small. The course is afebrile and the weight is stationary.

In view of the stationary condition, the lung involvement on the right and mostly at the base and roots, the negative sputum, the positive Wassermann, the comfortable feeling in spite of excavations, the afebrile course, the stationary weight and the typical location of luetic affection in the roentgenogram, the inference was that the case was one of syphilis and not of tuberculosis.

A similar case, with a clinical diagnosis of incipient tuberculosis,

showed the following roentgen findings: The entire left lung showed markedly diminished aeration apparently due to diffuse peribronchial infiltration, most marked at and around the hilus and along the left border of the heart toward the base. The right lung failed to show any changes, except for a few small calcified glands around the hilus. Almost all the costal cartilages appeared calcified. There was bulging of the right diaphragm. The ascending aorta appeared dilated.

The following facts appeared sufficient proof for diagnosing this case as syphilis of the lung rather than tuberculosis: (1) Stationary condition of the lung instead of rapid tissue destruction; (2) stationary general condition instead of emaciation; (3) repeated negative sputum; (4) repeated positive Wassermann; (5) development of interstitial keratitis with improvement on mixed treatment; (6) roentgen findings showing that the roots were mainly involved and that the ascending aorta was dilated.

From a humanitarian point of view, Bauch suggests the advisability of beginning the treatment of doubtful tuberculous cases with antisiphilitic remedies instead of waiting for gummatous ulcerations or excavations to develop, when the antisiphilitic treatment does little good.

Roentgen diagnosis of lung syphilis also forms the subject of an article by Watkins.<sup>55</sup> He refers to Stanley who describes three forms of lung syphilis, which Watkins finds will be recognized in the roentgenographic plates. Stanley describes these divisions as follows: The first class deals with early effects and produces an intense cell proliferation, filling the alveoli and infiltrating the septa, peribronchial, subpleural and perivascular tissues.

This, according to Watkins, presents on the roentgenogram a massive shadow, involving either an entire lobe or a large portion of a lobe contiguous to the mediastinum, and diminishing in density toward the periphery.

The second variety distinguished by Stanley is called by him early diffuse sclerosis, in which the lung looks and feels tough but is not misshapen. It is intensely mottled in places and shows great increase in connective tissue, especially in proliferating elastic tissue. Small miliary gummas are sometimes found. The roentgenogram which Watkins has found characteristic of this class represents

an evenly distributed, radiating, linear marking, or a diffuse speckling throughout the lung, sometimes bilateral.

The third form is a dense sclerosis, in which the lung may be contracted or misshapen, while the pleura, whether adherent or not, is much thickened. The proper structures of the lung are destroyed or distorted. The alveoli are made out with difficulty on account of the general condensation. In some places there is some emphysema and there is great increase of elastic fibers. Miliary gummas and vascular changes are common. Watkins' roentgenogram of this type has a characteristic pyramidal shadow with lancelike projections into the lung substance. This shadow is to be looked for in the lower or middle lobe, and not in the apex or upper lobe, as in tuberculosis.

Watkins selects five cases to demonstrate the typical roentgen marking of lung syphilis, in three of which the suggestion of syphilis was made by the roentgenogram, and this was subsequently confirmed by the clinical course and the laboratory diagnosis. He advocates the routine Wassermann test for all tuberculous patients, as not less than 15 per cent in approximately 1,000 chest roentgenograms showed the combined presence of syphilis and tuberculosis.

As to differentiation, Watkins states that lung syphilis must be differentiated from bronchiectasis, abscess, malignant tumors, pneumonokoniosis, unresolved pneumonia and tuberculosis. Bronchiectasis and abscess should not easily be mistaken for syphilis, since in them the cavity is a characteristic, while in syphilis absence of cavities is a peculiarity.

The lung shadow of pneumonokoniosis resembles that of combined syphilis and tuberculosis, and the probabilities are that any pneumonokoniotic patient with a positive Wassermann will have some foci of syphilis in the lung.

No roentgenologic differentiation can be made between lung syphilis and unresolved pneumonia, and the diagnosis depends on the clinical history and laboratory findings.

The recognition of differences between the shadows of syphilis and tuberculosis requires an intimate knowledge of the essential pathology of the two affections and their pathways of invasion into the lung. The shadows tend to show that syphilis invades the lower and middle lobes (contrary to Landis' statement), and tuberculosis



the upper. In syphilis the densest shadow begins at the hilum and diminishes toward the periphery, while in tuberculosis characteristic shadows surround the apical or subpleural lobules. The shadows do not bear a distinct relation to the bronchi in syphilis, while those of tuberculosis are perilobular and show a definite relation to some branch of the bronchial tree.

Syphilitic manifestations in the lungs, resembling pulmonary tuberculosis have also been observed by Daniells and Dachtler.<sup>29</sup> In a study of 150 cases of suspected tuberculosis of the lungs, extending over a period of ten years, the roentgenograms disclosed mixed infection of tuberculosis and syphilis in a few cases, while in eight cases the lung changes were due to syphilis. In all the cases tuberculosis was eliminated by Koch's tuberculin and by the fact that no signs of tuberculosis were demonstrated roentgenologically. On the other hand, the syphilitic infection was established by the history, clinical signs, Wassermann reaction and antisyphilitic treatment.

The roentgen findings for syphilis of the lung were hardly characteristic, and their greatest value was in excluding tuberculosis. From a study of these cases the authors believe that a syphilitic condition of the lungs occurs more frequently than is usually suspected and that without doubt it is often treated for pulmonary tuberculosis.

Callender<sup>11</sup> affirms that pulmonary syphilis gives a roentgen picture quite distinct from that of phthisis. The shadows, as in the same disease in bone, are clear-cut and sharp, with no tendency to mossiness of the borders and can be readily diagnosed by the roentgenogram. This is denied by Watkins<sup>55</sup> who states that the shadow of syphilis has a very irregular border and that for this reason it can not be mistaken for cancer, which gives a shadow with a sharp margin. In tumors of the lung the shadows are, according to Callender, homogeneous in appearance and lack the linear marking of the tuberculous lesion. The picture is quite distinct, especially in advanced conditions, and once seen can be easily diagnosed.

Moore and Carman<sup>44</sup> quote Rothschild as stating that pulmonary syphilis is shown in the roentgenograms as a diffuse shadow, but they have not seen any proved cases of pulmonary gumma, the pos-

sibility of syphilis having always been excluded by the Wassermann test.

Post<sup>51</sup> reports two cases of syphilis of the lung, accompanied by roentgenograms. In both the dark shadow is confined to one side and the heart drawn toward the affected side. Both patients were syphilitic and in neither were tubercle bacilli found. The author adds that diseases of the lung, in which consolidation is found in unusual positions, or limited entirely to one lung in which tubercle bacilli have not been found, may be considered suspicious of syphilis. If the Wassermann is positive, the suspicion is much greater and may almost be regarded as a certainty. A diagnosis of tuberculosis under such conditions would not be permissible.

Holmes<sup>34</sup> admits that syphilis of the lung is not well understood, although some types are fairly characteristic. Such is the case, when one lung is largely involved without infection of the other, as this is not usually seen in tuberculosis. Moreover, in characteristic roentgenograms of acute syphilitic infections the changes are most evident around the larger bronchi and are less sharply defined than in tuberculosis. Calcification may not be present and the periphery of the lung is not involved.

#### SYPHILIS OF THE STOMACH

Turning to syphilis of the stomach in its roentgenologic aspects: In a previous article Carman<sup>14</sup> has stated that the clinical symptoms of gastric syphilis alone are not sufficient to distinguish it from other organic or even functional disorders of the stomach, nor are the roentgen signs of themselves distinctive and pathognomonic. However, they furnish decisive evidence of gastric pathology and, in correlation with the clinical and laboratory findings, give indispensable aid in arriving at a diagnosis. In describing the roentgenologic characteristics of gastric syphilis, he has given special attention to the differentiation from cancer, stating that, if the filling defect is associated with a corresponding palpable mass, the whole picture would be easily mistaken for cancer but for considerations as follows:

1. Notwithstanding the extensive distortion of the stomach, no corresponding mass may be felt, and the filling defects are evidently

due, not to the intrusion of a tumor, but to an infiltration and contraction of the gastric walls.

2. The roentgenologist may be impressed by the discrepancy between the extent of gastric involvement and the general condition of the patient who is often below the cancer age, is anemic rather than cachectic, gives a longer history than that commonly given by cancer patients and, on the whole, is not ill in proportion to the extent of sickness as shown by the roentgen ray.

3. The infrequency of a six-hour residue of the barium meal in syphilis is noteworthy. While in cancer of the stomach the six-hour retention occurs in 60 per cent of the cases, and in gastric ulcer in 50 per cent, such residue is only rarely seen in syphilis of the stomach. But even with these points in favor of a diagnosis of gastric syphilis, the latter should be confirmed by a Wassermann test and examination of the spinal fluid.

Since this article was written, the writer's experience has been that in many of these cases the roentgen findings which had previously only been noticed as important enough for further study and observation, positively furnish characteristic information on which a roentgen diagnosis may be based. The points are precisely those mentioned in this article, and the writer has convinced himself that they furnish reliable guides. This does not mean that he would commit himself to 100 per cent correct diagnoses, but among the cases which have since come under his notice there have been several, in which a diagnosis of gastric syphilis was made on the strength of the roentgen findings alone, such diagnoses having been afterward confirmed by the clinical history, serologic tests and the effect of specific treatment.

Thus, although it is perfectly true that, up to a short time ago, syphilis of the stomach was more or less of a curiosity, nevertheless the more recent experience and studies of Downes, Le Wald, the writer, and others, have culminated in the fact that the symptomatology and the methods of roentgenologic examination have been fairly thoroughly worked out. It is not easy to understand why there should be such a discrepancy between clinicians and pathologists about this disease except on the assumption that patients regain their health and there is no opportunity for postmortem verification.

McNeil's<sup>41</sup> opinion on syphilis of the stomach was formed at a time when practically all pathologists, as he states, seemed to consider it more or less of a curiosity.

On the other hand, Eusterman<sup>29</sup> believes that the affection, though rare, is not as infrequent as is generally supposed. The possibility of its presence should be considered in every atypical case and the diagnosis may often be accidental, but the aid of the Wassermann reaction and the roentgen rays is necessary to establish the specificity of the lesion. The fallacy should be avoided of considering a gastric lesion necessarily luetic in the presence of a consistently positive Wassermann, because syphilis may coexist with benign and malignant gastric disease. The role played by syphilis in the etiology of gastric ulcer is doubtful not only because of the rarity of the cases in which the two are associated, but also because of the results of Rosenow's research work in regard to the streptococcal origin of gastric and duodenal ulcers, and finally, because of insufficient evidence to show that simple ulcer becomes gummatous in the presence of systemic or gastric syphilis. The author therefore considers the inclusion of roentgenology in the methods of examination as absolutely necessary to make an accurate differentiation between early syphilitic gastric ulcer and nonseptic lesions of the stomach. To the roentgenologist, the combination of a gross filling defect in the absence of a palpable mass and 6-hour barium residue, the tendency to hourglass deformity and the absence of a proportionate cachexia, suggest gastric syphilis. Technically, however, the author adds, such findings can not be differentiated from carcinoma.

Einhorn,<sup>26</sup> in his further observations (1915) on this subject, includes the interesting report of a case of syphilitic tumor of the stomach which simulated cancer to the minutest detail. This refers not only to the clinical symptoms but also to the roentgen examination. The patient was a 46-year-old negro, and the first roentgenologic report simply stated that there were symptoms of indurated pyloric ulcer. The report of a second examination six days later read as follows: "Partial defect in the pyloric part, stomach vertical, orthotonic. No residue after six hours. Intestinal hypermotility. Pylorus at the level of the umbilicus in the median line. The lesser curvature on the left of the median line."

The roentgen diagnosis was, therefore, carcinoma of the pylorus. As the Wassermann reaction was strongly positive, the patient was treated on antisyphilitic principles with complete success.

In another case the roentgen examination confirmed the clinical diagnosis of a dilated stomach and some irregularity of the duodenal cap, but was not sufficiently definite to justify a diagnosis. Large doses of bismuth and atropin failed to relieve the periodic attacks of severe vomiting, and gastroenterostomy was already considered when, on account of the positive Wassermann reaction, antisyphilitic treatment was applied, which brought about a complete recovery.

A case of syphilitic hourglass contraction is within the experience of Culler.<sup>19</sup> The patient, a man of 44 years, had contracted a sore seventeen years previously, which was cured by local treatment. Ten years later a gumma appeared on the tibia, following a slight traumatism. No further trouble occurred until recently, when, aside from a severe iritis, there were indigestion, vomiting, pain and tenderness in the epigastrium. This condition was diagnosed by several physicians as gastric or duodenal ulcer, and not until the roentgen and Wassermann examinations were made was the correct diagnosis of hourglass contracture of the stomach, due to syphilitic ulceration, established.

Downes<sup>24</sup> sends in a "Further Report of Eight Cases of Syphilis of the Stomach," which is an amplified rendition of the report by Downes and LeWald<sup>23</sup> of over two years previously. According to these authors the diagnosis of syphilis of the stomach can be made with a fair degree of certainty, if the clinical and laboratory findings are given proper consideration. Acquired cases may be more difficult to diagnose than the congenital, but in both types the course of the disease differs from the simple gastric or duodenal ulcer. A positive Wassermann reaction with roentgenographic findings of persistent and unusual deformity of the stomach establishes the diagnosis beyond much doubt, although the value of the antisyphilitic treatment in confirming the diagnosis can not be ignored. In two of the author's cases a pathologic diagnosis could not be made even from the laboratory specimens, because they were negative for tubercle bacilli as well as for *Spirochetes pallida*. As all gastric ulcers, syphilitic or otherwise, have potential dangers,

excision and resection should be considered in every suitable case. But since syphilis of the stomach is only the local evidence of a general disease, no patient should be subjected to more than the simplest form of operation, until after the antiluetic treatment has been given a trial. Thus, in three of their eight cases the relief from symptoms was so satisfactory under appropriate treatment that no operation was resorted to, and all the patients have done well for periods of from two years to three years and six months, with the exception of one patient who died of Bright's disease a year after the diagnosis of syphilis had been made.

The roentgenograms showed the following characteristic signs: In the congenital affection of a 14-year-old girl there was a dumb-bell-shaped prominence due to sclerosis of the body of the stomach. After gastroenterostomy most of the food passed through the opening, but enough passed through the stenosed portion to outline it. There was compensatory dilatation of the esophagus.

In the case of a woman, 34 years of age, there was an hourglass constriction with a long channel between pouches which was relieved by operation. In a younger woman there was deformity at the pyloric third of the stomach due to sclerosis, closely resembling a new growth. A diagnosis of syphilis was microscopically confirmed and the symptoms relieved by gastroenterostomy, but the deformity persisted.

The congenital case of a boy, 17 years old, with a deformity at the juncture of the pyloric and middle thirds of the stomach, responded to medical treatment but the deformity remained. Another case that responded to medical treatment was that of a 62-year-old man with deformity of the body of the stomach and the pyloric region, due to sclerosis. The small stomach emptied rapidly three minutes after a full bismuth meal, and the duodenum was completely filled. Two years later the stomach capacity was larger and emptying occurred less rapidly.

Almost identical conditions prevailed in a young woman of 23 years, who was treated medically with success, although the deformity remained. Here there was compensatory dilatation of the esophagus to make up for the small size of the stomach. A similar improvement is shown by the roentgenogram of the last of the eight cases, made two and a half years after treatment.

The author concludes his paper by reflecting on the tendency for every case of syphilis to relapse, however well treated, and he can not therefore expect these patients to remain permanently free of gastric symptoms; but the fact remains that the diagnosis must be assumed to have been correct, since the symptoms have been controlled and the patients "clinically cured."

A clinical study of twenty-six cases of dyspepsia, associated with positive Wassermann-Noguchi reactions, is contributed to the literature by Smithies.<sup>53</sup> This report comprises observations on twenty-six dyspeptic persons whose clinical history was definite or highly probable, or in whom an exploratory laparotomy had demonstrated atypical gastric conditions. Under such circumstances the result of the roentgen examinations are of particular interest.

According to Smithies three divisions with regard to the clinical course of the dyspepsia have to be considered: (1) When a persistent gastric derangement appeared in persons who had previously experienced no digestive upset; (2) when a constant dyspepsia followed years of antecedent indigestion of the intermittent type; (3) when continuous gastric upsets arose in patients who had been affected gastrically at some past period but who had been for years free from digestive disturbances.

*Group 1.*—This consisted of two cases, one of which was associated with epigastric nodule. In this case the fluoroscopic examination disclosed a filling defect of the pylorus and antrum. In the other case roentgenoscopy pointed to a probable pyloric ulcer of the chronic, uncomplicated variety.

*Group 2.*—This was made up of ten cases, in eight of which roentgenoscopy returned the diagnosis of chronic peptic ulcer, suspicious ulcer, or "tumor" of the stomach. Without the knowledge of specific infection or positive serologic test, a clinical differentiation from ordinary recurrent gastric ulcer is quite impossible on account of the close similarity of the symptoms and signs.

*Group 3.*—A roentgen record of an intragastric condition simulating chronic ulcer or tumor was obtained in nine cases of the fourteen that composed this group. In the remaining instances the examination was not made or its result was questionable.

From these results Smithies has come to the conclusion that in these groups of syphilitic gastric infection neither screen nor plates

usually return pathognomonic signs. The roentgen method may ocularly demonstrate deformities in gastric contour, but in the main such deviations from the normal might readily be observed in benign or malignant peptic ulcer and carcinoma, scirrhus or medullary. It seems to him that a roentgen sign of some value might be deduced from the rather anomalous findings of a gastric tumor or extensive deformity, associated with fairly high degrees of peristalsis and with test meal returns showing normal, or slightly reduced free hydrochloric acid. With a concomitant positive Wassermann-Noguchi reaction the diagnosis is reasonably certain. Besides, certain roentgen signs may be suggestive enough to lead to the making of serologic tests and the beginning of specific therapy.

Since writing the foregoing, Smithies does not appear to have changed his views on the value of roentgenology in gastric syphilis. A further article on syphilis of the stomach<sup>52</sup> describes the study of thirty-five cases of organic gastric lesions, associated with positive Wassermann-Noguchi reactions. Although the bulk of the author's observations are of a clinical nature, he found that the roentgen demonstration of gastric deformity is of much service in doubtful cases. He states that usually neither fluoroscopy nor plates reveal pathologic signs. They may demonstrate deformities in gastric contour, but such deviations might also be observed in benign or malignant peptic ulcer and carcinoma. In the absence of hourglass deformity, rapid emptying may occur, while in its presence the opaque meal may lag in one loculus with early emptying of the other. Crater ulcers not infrequently exhibit local retention flecks which may be multiple. Such are rather characteristic, inasmuch as nonlucetic gastric ulcer is seldom multiple. A roentgen sign of some worth might be seen in the rather anomalous findings of a gastric tumor or extensive deformity, associated with a fairly high degree of peristalsis and normal or slightly reduced hydrochloric acid.

The late Hunter McGuire is said to have stated that much of his success was due to treating patients for syphilis whenever their manifestations were obscure. In fact, Niles<sup>47</sup> believes the same principle might apply with satisfaction to some of our long-suffering dyspeptics who have run the therapeutic gamut without relief. Niles reports a case in which the feature of interest was the difficulty to



differentiate between cancer and syphilis of the stomach. Even the roentgenogram, unless interpreted in conjunction with the clinical investigation and the positive Wassermann, would have been misleading.

In a group of 600 cases of syphilis with strongly positive Wassermann, White<sup>50</sup> found forty-four with prominent gastric symptoms, after excluding patients with hepatic cirrhosis, gumma of the liver, nephritis and tabes. Two cases were proved by necropsy to be cancer of the stomach, but during life it was absolutely impossible to make a positive diagnosis between syphilis and cancer by history, physical examination, lack of gastric secretion, roentgen ray defect or even the appearance of the stomach at operation. In such doubtful cases a relatively benign course and the combination of quite good health with a large stomach lesion, which is often best shown by the roentgen examination, suggests syphilis. However, the author adds that the diagnosis of syphilis of the stomach has not been and will not be absolute as a rule. Even the relief of symptoms by treatment is not a sure guide in diagnosis, although the roentgen demonstration of plaques, large indurated areas, hourglass deformity or tumors, is valuable evidence that the lesion is specific, especially if in the presence of a positive Wassermann these symptoms disappear under antisyphilitic treatment.

The roentgen rays have proved of great value in locating the lesions exactly and following their changes under treatment accurately. It is no longer necessary to depend on the palpation of a rare tumor and its disappearance under the finger.

Dewis<sup>22</sup> holds that syphilis of the stomach is uncommon and holds that the first clue to this lesion is a history of infection, confirmed by the Wassermann test and the roentgen ray, the latter being most valuable in the differential diagnosis. The roentgenograms he has seen did not have the moth-eaten appearance of cancer, and there was much more extensive involvement of the stomach wall than in simple ulcer. In syphilitic ulcer there seemed to be a strong tendency to the production of an hourglass deformity, and in connection therewith he has noted what appears to be a very important characteristic point which differentiates it from cancer and simple ulcer. In describing his observations, Dewis states that in syphilitic hourglass of the stomach we see a long regular isthmus, at each end

of which the walls of the stomach rise more or less abruptly or dumb-bell-like. This is in contrast to the sharp incision of simple ulcer hourglass with practically no isthmus; and the picture differs quite as much from the cancer hourglass, with the infiltrated walls of the stomach sloping irregularly away from the constricted portion.

During the last three years LeWald<sup>38</sup> has studied 19 cases of gastric syphilis with, and 4 cases without, a positive Wassermann reaction. The roentgen findings may be classified as follows:

1. Diminished size.
2. Dumb-bell-shaped deformity (hourglass stomach), due to stenosis of the middle of the stomach; in this type there is apt to be dilatation of the esophagus.
3. Infiltration of the pyloric region, with or without dilatation of the stomach and retention.
4. Filling defects about the greater curvature or in any other portion of the stomach.

Roentgen examination and Wassermann reaction provide the necessary data on which to make the diagnosis in doubtful cases, and they should never be omitted. Congenital cases may escape diagnosis owing to the fact that syphilis may not be suspected.

Mühlmann<sup>46</sup> describes the case of a young married woman with acquired syphilis, in whom gastric disturbances developed four or five years later. The syndrome was typical for contracted stomach, apparent slight capacity of the stomach which resented overeating by violent vomiting, in spite of which the patient was always hungry. The Wassermann was still positive. The first roentgen examination showed a very small stomach without peristalsis, but with constant retractions simulating peristaltic waves. There was slight regurgitation into the esophagus. The opaque meal flowed out slowly but continuously through the persistently patent, very narrow pylorus. Diagnosis: Contracted stomach due to syphilitic sclerosis.

The second roentgen examination, after gastroenterostomy, did not differ from the first except that the gastroenterostomy loops were in active motion. There was still slight regurgitation into the esophagus. A third roentgen examination, nine months later, showed the shape of the stomach unchanged, with functioning gastroenterostomy. There was fusiform dilatation of the lower third of the esophagus.

Comparing this case with three other reported cases of Johann Mueller, Eppinger and Schwarz, Hemmeter and Stokes, the author finds a syndrome which may be narrowed down to two principal points; syphilis, and contracted stomach with dyspeptic manifestations. He does not mean to say that every positive Wassermann case is etiologically related to an intercurrent gastric affection, associated with stormy vomiting. But the connecting link is either furnished by the roentgenologic demonstration of a contracted stomach or, failing this, by the demonstration of abnormal peristalsis pointing to an incipient infiltration of the wall.

#### SYPHILIS OF THE DUODENUM

Syphilis of the duodenum has been observed by Mortimer<sup>45</sup> who appreciates the valuable aid of the Wassermann reaction and the roentgen ray in recognizing more cases of intestinal syphilis during the earlier stages, before permanent destructive changes have occurred. He reports the case of a widow, 37 years of age, who gave birth to a syphilitic child. The husband died of paresis. The Wassermann reaction was positive, and there was a hard, irregular mass in the right hypochondrium. There was occult blood. Under antisiphilitic therapy there was improvement of the general condition and diminution in the size of the tumor.

The fluoroscopic examination showed a rapidly filling stomach, which was enlarged, the greater curvature being about 2 inches below the umbilicus. The peristaltic waves were rapid and of moderate depth. Within a few minutes the postpyloric region was visualized, showing a narrow, irregular filling defect, which persisted. The duodenal cap was distorted. No six-hour residue was seen.

#### SYPHILIS OF THE RECTUM

Rectal syphilis is a lesion rarely encountered, at least in roentgenologic practice. But as Case<sup>15</sup> states, the appearance of this lesion at the time of the rectal injection is so characteristic that, once seen, it can never be forgotten. His article is accompanied by an illustration of a case. The rectal channel is converted into a narrow canal, more or less elongated, according to the extent of the lesion. The first portion of the injected material shoots up this narrow canal with astonishing rapidity. In the cases he has recog-

nized in his practice, the filling defect was smooth-edged and more extensive than in any malignant lesion he has yet seen in a living patient. Probably a good many syphilitic lesions of the rectum are being mistaken for malignant disease, and it is not uncommon for the error to be discovered after surgical excision has been made.

Referring generally to the value of roentgenology in the diagnosis of syphilitic and other malignant disease, it is not so very long ago that Brickner wrote editorially in the *American Journal of Surgery*,<sup>8</sup> and repeated the statement six months later,<sup>9</sup> that the roentgenograms of a pathologic fracture of a long bone may suggest a gumma, a sarcoma, or a carcinoma, so that a roentgenologist not very alert and experienced is apt to make the wrong diagnosis and on his report a patient may be submitted to an unnecessary operation for sarcoma who should have been treated by salvarsan and mercury. If the surgeon's attention has once been called to the possibility of a syphilitic infection he will weigh these findings with all the other available evidences and tests before performing the operation. No doubt there are competent and incompetent roentgenologists, but Brickner himself admits in a different paragraph that "the radiographic features of bone syphilis are so characteristic that in most cases the diagnosis can be made from the x-ray plate alone."

Brown<sup>10</sup> believes that the real use of roentgen rays in the general diagnosis of hereditary stigmas consists in the prominent part they should play in the general diagnostic overhauling, for instance, in the case of children who present the slightest evidence of such signs in the form of subjective symptoms which can not be locally unaccounted for. Thus, he refers to photophobia or any other ophthalmic manifestation; headache, snuffles, sore legs, mental backwardness, skeletal asymmetries, etc. Syphilis in its acquired form will ever be a source of interest to the roentgenologist, but Brown predicts that the hereditary types will supersede it.

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## THE DIAGNOSIS AND TREATMENT OF SYPHILIS IN MEN

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THE increase of syphilis made evident since the entry of the United States into the World War serves as sufficient reason to publish this report of the diagnosis and treatment of luetic men, most of whom were in the age group for either recruiting or drafting.

The great temptation in syphilis at present is to let the other fellow make the diagnosis. Since the laboratory has evolved a diagnostic method that is enlightening in lues, the clinician has all too readily been willing to accept laboratory diagnoses, and physical observation has gone by the board. Even the specialist has fallen prey to the tendency of the times. The keen differential diagnosis of specific and nonspecific skin lesions becomes a lost art, and taking blood for a Wassermann test is substituted. This procedure is absolutely pernicious, especially in suspicious primary lesions, because the blood may give a negative reaction and the patient still be in an active syphilitic stage when the disease may be aborted.

Undoubtedly the Wassermann reaction is the greatest diagnostic tool in syphilis in the possession of the medical profession today. Like every other route to diagnosis, however, it should be used only in conjunction with other findings. The evidence that for centuries prior to serologic knowledge gave the clinician his diagnosis should not be neglected. Observation stood first in those days, history second.

Complete inhibition of complement, usually reported as four-plus (++++), positive undoubtedly means the patient has or has had active syphilis. The so-called paradoxical reaction, or nonspecific (++++), occurs in yaws, sleeping sickness, malaria, trichinosis, and



the nodular form of leprosy. Slightly positive reactions may occur in tuberculosis, and perhaps in measles and scarlet fever.

The New York Board of Health advisably states on the back of each report:

## INTERPRETATION OF THE WASSERMANN READINGS

++++	means very strongly positive
+++	“ strongly positive
++	“ positive
+	“ weakly positive
±	“ doubtful
-	“ negative

A diagnosis of syphilis should never be made from a weakly positive or doubtful reaction (+ or ±), but in a known case of syphilis that has had specific treatment, such a reaction would indicate the necessity of further treatment.

A weakly positive or doubtful reaction (+ or ±) where there is no specific history and where the test is made simply as an aid in differential diagnosis, is usually considered as negative. A negative Wassermann reaction does not absolutely exclude the possibility of syphilitic infection.

The warning is not taken in every instance. Several patients have come to us with histories of having had a weakly positive Wassermann and having been treated for syphilis. We were never able to find clinical or serologic evidence of lues in these patients, and in the absence of history concluded that they had never had the disease. Contrariwise, patients have brought us negative Wassermann reports on blood taken during the primary stage. Their physicians on this ground ruled out syphilis, yet on physical examination one such patient revealed a generalized macular syphilide.

The value of the Wassermann reaction during specific therapy in a known luetic will be considered later on in this paper.

The clinician should make himself expert in diagnosing active lues, and become independent of the laboratory. The bacteriology of syphilis has so developed that the demonstration of the causative spirochete means that the patient has syphilis. Every penile lesion and any suspicious extragenital sore should be examined for *treponema pallidum*. The primary lesion of syphilis may simulate any and every variety of nonspecific sore. Even experienced clinicians are led into making nonluetic diagnoses of syphilitic chancres. We have found spirochete pallida in the most innocent appearing her-

petic vesicle, and in a pea-sized papule that four days previous had been a vesicle. We have notes on several cases where the patient went to a physician with a vesicle, which was diagnosed as herpes progenitalis. While under treatment the lesion ulcerated, yet the treatment remained nonspecific until the secondaries appeared. Another type of chancre not ordinarily recognized clinically is the erosive chancre. This usually occurs on the glans penis, and simulates balanoposthitis. Of course, bacterial diagnosis in these cases is rendered especially interesting because of the necessity of differentiating spirochete pallida from nonspecific spiral organisms. Puncture of the locally enlarged lymph nodes is recommended in these cases. The type of lesion named after Hunter, the indurated ulcerative chancre, is readily diagnosed. It must not be forgotten, however, that cauterization of any lesion may give an induration which simulates the cartilaginous character of the Hunterian chancre.

We use as routine the dark-field method for the demonstration of the spirochete pallida. The apparatus required are: microscope, oil immersion lens containing the essential "funnel stop," a dark-field condenser, and a powerful light. The miniature arc light and the tungsten bulb inclosed in a special reflector made by Leitz have both been found satisfactory by us. Ten minutes' demonstration is worth hours of description in setting up the instrument, obtaining material for examination, and the recognition of the specific organism. Complete observations on the subject will occupy us at some future time.

We note with some concern the relatively few cases of primary lesions without secondary manifestations that present themselves. The optimism that pervades those afflicted with disease is prevalent but sadly misplaced in our class of patients. Any explanation keeps the patient satisfied and away from the doctor. A frenum torn by coitus; the woman was menstruating, or about to, or had just menstruated; excessive masturbation; and physical injury have all been given as the cause of a penile lesion. The long incubation time gives an opportunity for many patients to forget a casual and causal relation. The patient's version of affairs is too often accepted by the doctor he finally consults. The dark-field or India ink methods are not used, and the man is sent away assured that

he has a local disease easily cured. A blood test may be taken, and if negative, as it is early in the disease, double assurance is given that lues is absent. The idea that luetic chancres are "hard" chancres is still prevalent and confuses many. The textbook Hunterian chancre is not the only initial lesion that harbors the spirochete of syphilis. The hard and fast rule regarding the three weeks incubation period adds confusion. The men of the class under our care are seldom free from exposure for so long a time and are likely to do give the date of the last exposure prior to the appearance of a penile lesion as the incubation time. This will ordinarily be two or three days, the incubation time of soft chancre or chancroid. The fact that for an altogether unknown reason no case of chancroid due to the Ducrey bacillus has been to us for two years does not deter doctors from making this diagnosis on clinical evidence alone. It can not be repeated too often that a few moments' search in an untreated lesion would clear the diagnosis.

I wish merely to mention the passing of the chancroid, at least in New York. We have questioned many men who have opportunities both in clinic and private practice for observation and they are unanimous in saying that they have not seen a case in several years. Clinicians from Southern ports tell us that they have them as numerous as before. The bugaboo of the mixed sore ought now to die a natural death. Its toll in untreated syphilitics has reached enormous numbers during its reign, and among the uninitiated still satisfies the conscience of those who gave a good prognosis for a penile sore which cleared up nicely but whose possessor a month later was covered with secondaries.

We have observed during the period from June, 1916, to October, 1917, fifteen cases of primary syphilis with negative Wassermann reaction and no evidence of secondaries. Six of these had a full course of salvarsan and none of these developed positive reactions or secondary symptoms. Two of these cases were infected by the same woman, and both presented the ulcerative indurated type of chancre, about the size of a pea at the first visit. The duration was from nine to four days in all of these cases but one, in which the lesion was present seventeen days. The diagnosis was always controlled by the demonstration of the spirochete pallida.

A representative history of this type of case reads as follows:

REPORT I.—Name, Br. Age, 25. Date, Oct. 7, 1916.

*Diagnosis.*—Primary syphilis.

Spirochete pallida demonstrated in lesion of nine days.

WASSERMANN	SALVARSAN	MERCURY
Oct. 7, 1916, neg.	Oct. to Dec., 1916, 6 doses	20 injections
Jan. 29, 1917, neg.	Jan. to Mar., 1917, 7 doses	
Feb. 27, 1917, neg.	Apr. 10, 1917, provocative	
Apr. 10, 1917, neg.		
Apr. 11, 1917, neg. (Provoe)		
July 31, 1917, neg.		

A case of syphilis treated while still a local disease. Chancre, no secondaries, and a negative Wassermann. Therapeutic attack is successful. Patient absolutely rid of the disease. True example of "abortive cure."

We observed another primary case that was very instructive. When first seen, he presented an ulcerative lesion of the glans. The dark-field demonstrated the spirochete pallida. Mercury salicylate was given immediately, and he was instructed to prepare for salvarsan the next Tuesday. Blood for a Wassermann was taken which was reported negative the following Friday. The patient did not return until ten days later when the blood was taken again. This sample was reported ++++ positive and confirmed our diagnosis of the type of organism we demonstrated in the lesion. The full history follows:

REPORT II.—Name, Cu. Age, 35. Date, March 20, 1917.

*Diagnosis.*—Primary syphilis.

Clinical diagnosis confirmed by the demonstration of the spirochete pallida. Duration of lesion about ten days.

WASSERMANN	SALVARSAN	MERCURY SALICYLATE
Mar. 20, 1917, neg.	Mar. 27, 1917	30 injections
Mar. 30, 1917, ++++	Apr. 3, 1917	
Apr. 10, 1917, ++++	Apr. 10, 1917	
May 11, 1917, neg.	Apr. 17, 1917	
July 10, 1917, neg.	May 1, 1917	
	May 15, 1917	
	July 10, 1917	
	July 17, 1917	
	Aug. 14, 1917	
	Sept. 4, 1917	

Case observed in chancre stage prior to generalization. Began salvarsan week later at which time Wassermann reaction was already ++++ positive. Disease readily amenable to treatment. Ultimate cure assured. Provocative salvarsan not yet given.

A comparatively large number of our cases come to us with primary lesions, no evidence of secondaries either of skin or mucous membranes, yet the Wassermann reaction is reported ++++ or occasionally +++. This period of the syphilitic attack on the human economy, we have termed the "silent generalization stage." The cases such as these which remain under treatment with salvarsan and mercury are for the most part readily cured clinically and serologically, but there are exceptions. The case reports which follow are of especial interest.

Two boys came in October, 1916, with initial lesions of syphilis. The history given was that these sores had been acquired a month previously by pederasty. The incubation was indefinite since they were exposed over a period of six weeks. Despite the month's duration, there was no evidence of secondaries, but the Wassermann was already ++++ positive. The boys came together regularly for treatment, but the serologic findings were widely divergent. In the more favorable case Lu., physical examination disclosed a strong, short, stocky fellow of 145 pounds. Da. was a tall slim boy of 150 pounds. His heart was enlarged and there was evidence of a mitral stenosis and insufficiency with a history of acute articular disease as a child.

REPORT III.—Name, Lu. Age, 18. Date, Oct. 3, 1916.

*Diagnosis.*—Primary syphilis. Silent generalization stage.

Diagnosed clinically. Incubation unknown.

Duration, one month. Contracted from a man by pederasty.

No secondaries, but Wassermann ++++ on first visit.

WASSERMANN	SALVARSAN	MERCURY SALICYLATE
Oct. 10, 1916, ++++	Oct. to Dec., 1916, 8 doses	Weekly for ten
Jan. 9, 1917, +	Jan. to Mar., 1917, 6 doses	months except for
Feb. 13, 1917, neg.	Aug. 28, 1917, provocative	six weeks vacation.
Mar. 2, 1917, ++ (provoc)		
Mar. 20, 1917, neg.		
May 1, 1917, +		
July 10, 1917, neg.		

Aug. 7, 1917, neg.  
 Aug. 28, 1917, neg.  
 Aug. 29, 1917, neg (provoe)  
 Aug. 30, 1917, neg.

Disease recognized in silent generalization stage. Thorough treatment with salvarsan and mercury. No evidence of visceral or arterial disease. Provocative Wassermanns negative after salvarsan.

REPORT IV.—Name, Da. Age, 17. Date, Oct. 10, 1916.

*Diagnosis*.—Primary syphilis. Silent generalization stage.

Diagnosed clinically. Incubation unknown.

Duration, one month. Contracted from same man as Lu.

No secondaries, but Wassermann ++++ on first visit.

WASSERMANN	SALVARSAN	MERCURY SALICYLATE
Oct. 13, 1916, ++++	Oct. to Dec., 1916, 8 doses	Weekly for ten
Jan. 2, 1917, ++	Jan. to Mar., 1917, 5 doses	months except
Feb. 13, 1917, ++++	Aug. 28, 1917, provocative	six weeks
Mar. 2, 1917, ++		vacation
May 1, 1917, +		
July 10, 1917, ++		
Aug. 7, 1917, neg.		
Aug. 28, 1917, ++		
Aug. 29, 1917, +++ (provoe)		
Aug. 30, 1917, ++++		

Disease recognized in silent generalization stage. Duration, source, and treatment same as Lu., but a myocarditis from rheumatic infection delayed eradication of disease. No clinical evidence of cerebrospinal involvement. Poor example of provocative action of salvarsan because of positive Wassermann prior to injection. Rise from ++ to +++ to ++++ in three days is significant of the hold lues has on this patient's tissues. An ultimate cure is not assured in this case.

A third boy came who was exposed several times to infection from this same dangerous pervert. No sore had appeared and the blood Wassermann several months after the last exposure was negative. These cases recalled two old problems in syphilis. Why does not every one exposed to infection get the disease, and why once acquired, even from the same source, does the disease take various courses? We have found no better explanation than that used by Osler in speaking of the various manifestations of tuberculosis. The analogy of the "seed and the soil" fits both these scourges of the human race.

An exceptionally interesting case of lues observed in the silent generalization stage is the following:

REPORT V.—Name, Wa. W. Age, 21. Date, June 6, 1916.

*Diagnosis.*—Primary syphilis. Silent generalization stage.

Was circumcised elsewhere because sore present.

No hint given that this might be luetic. Came to us with acute gonorrhea and nonpainful adenopathy of groins. Wassermann + + + +.

WASSERMANN	SALVARSAN	MERCURY INJECTIONS
June 6, 1916, + + + +	June to Oct., 1916, 3 doses	Salicylate weekly
June 31, 1916, + + + +	Oct. to Dec., 1916, 1 dose	for twelve
Dec. 31, 1916, neg.	Jan. to Mar., 1917, 2 doses	months
Feb. 2, 1917, neg.	Apr. to June, 1917, 5 doses	

Patient began treatment in silent generalization stage. Secondary skin or mucous membrane lesions never developed. Interesting because of excision of the chancre prior to time when clinical diagnosis was possible, yet there was subsequent swelling of the local glands and spread of the syphilitic virus.

The next case is one that developed his secondaries despite several injections of mercury salicylate, although he was in the silent generalization stage on his first visit.

REPORT VI.—Name, Pa. Age, 29. Date, Oct. 24, 1916.

*Diagnosis.*—Primary syphilis. Generalization stage.

Incubation, one week. Duration, four weeks.

WASSERMANN	SALVARSAN	MERCURY
Oct. 27, 1916, + + + +	Oct. to Dec., 1916, 2 doses	Irregularly for
Aug. 3, 1917, neg.	Jan. to Mar., 1916, 1 dose	one year.
	Apr. to June, 1917, 9 doses	

Patient observed during silent generalization stage. Secondaries appear on third visit despite two injections of mercury salicylate. Salvarsan begun two weeks after, but only three doses administered in first six months of infection. Full course of salvarsan given in what is really the latent tertiary stage of syphilis. Ultimate prognosis favorable but will require observation over a long period of time. Provocative salvarsan will be enlightening in this case.

For comparison the next history is given:

REPORT VII.—Name, Mu. Age, 28. Date, Aug. 8, 1916.

*Diagnosis.*—Primary syphilis. Silent generalization stage.

Incubation, one week. Duration, three days (?).

WASSERMANN	SALVARSAN	MERCURY
Dec. 1, 1916, ++++	Aug. to Oct., 1916, 1 dose	Irregularly
Jan. 5, 1917, +	Oct. to Dec., 1916, 2 doses	about once
May 4, 1917, ++	Apr. to June, 1917, 1 dose	a month on
Oct 6, 1917, ++++	July to Oct., 1917, 1 dose	the average

Carelessness on the part of the patient permits infection to gain headway, although came under observation at a comparatively favorable time.

About one-half of our active syphilis cases come to us for the first time with the secondary eruption in full blast. In some the initial lesion had never been noted, or had already been forgotten. In others the patient had been under treatment for gonorrhea and in these cases we suspect an intraurethral chancre. We have seen three of these. Several men have come to us with the generalized eruption whose chancres had been diagnosed nonspecific and which had healed by local treatment. Patients come, too, with secondary syphilis who had drug store treatment of the chancre. The kind, public-serving druggist collected twenty-five cents for a box of calomel powder or ointment and set up another cycle of specific infection. How to limit the pharmacist, especially among the poorer classes, to his rightful dispensing function is part of the problem in the control of this disease.

One especially instructive case in this series came to our attention. A lad came with early gonorrhea. He remained for several visits and disappeared for several weeks, after which he returned. On his second visit, after the vacation, he had a generalized rash. No initial lesion could be found, nor was there any grounds for more than a suspicion of an intraurethral or rectal chancre. The patient had received copaiba, and it was thought that we were dealing with a medicinal eruption, but lues was the final clinical diagnosis. The absence of mouth lesions, or moist patches elsewhere made the demonstration of spirochetes a difficult task. The Wassermann test was done and reported ++++ positive. When interrogated very fully, we learned that during his absence from our clinic, he had been circumcised because two sores appeared on the foreskin. This case and that of Wa. (Report V) emphasized the necessity for spirochetal examination of all lesions, and the uselessness of excision of the chancre.

One case of secondary lues came to us with marked evidence of a severe attack on the cerebrospinal system. Unfortunately we had



no opportunity to study the spinal fluid of this man. I wish to refer to the splendid work of Fordyce whose studies have led him to conclude that the attack on the nervous system takes place in the secondary period of lues, although the manifestations as tabes or paresis may not be clinically evident for many years.

We give the detailed histories of a few patients first treated with salvarsan when they were in the active secondary stage.

REPORT VIII.—Name, Sm. Age, 25. Date, Dec. 19, 1916.

*Diagnosis.*—Secondary syphilis. Duration, unknown.

Chancre of foreskin. Incubation, three weeks. Duration, six weeks.

Adenopathy. Macular syphilide. Palmar lesions. Tremor. Unequal pupils. Jerky speech.

WASSERMANN	SALVARSAN	MERCURY
Dec. 19, 1916, ++++	Oct. to Dec., 1916, 1 dose	Regularly for
Mar. 7, 1917, neg.	Jan. to Mar., 1917, 11 doses	six months
July 31, 1917, neg.	Apr. to June, 1917, 3 doses	
	July to Oct., 1917, 4 doses	

Marked secondaries with evidence of severe attack on the nervous system. Eradication of the disease clinically with salvarsan intravenously and mercury by intramuscular injection. Serology favorable but not observed sufficiently long after cessation of treatment to be reliable.

REPORT IX.—Name, Su., Jas. Age, 28. Date, Sept. 16, 1916.

*Diagnosis.*—Secondary syphilis. Duration, unknown.

Chancre, May, 1916.

WASSERMANN	SALVARSAN	MERCURY
Sept. 16, 1916, ++++	Jan. to Mar., 1917, 3 doses	25 injections
Dec. 1, 1916, +	Apr. to June, 1917, 3 doses	
Feb. 23, 1917, neg.		
Apr. 17, 1917, neg.		

Wassermann reduced from ++++ to + by 17 injections of mercury salicylate. Blood twice negative during treatment with salvarsan. Further observation necessary before one can speak of cure in such cases, but may call this a successful therapeutic attack.

About half of our cases are past the active secondary stage and are without clinical symptoms. This phase of lues is the latent tertiary period. Some of these patients were observed in previous years, and their complete histories are available for study. Others

are new, and we have less accurate data concerning them. The character and quantity of former treatment varies from cauterization of the chancre and a few bottles of mixed treatment, to persistent courses of mercury by injection over a long period of years. Less complimentary to our colleagues are cases pronounced cured in our own day of salvarsan and the Wassermann. This group came to us with reports of four-plus Wassermann taken routinely by the Board of Health on waiters, bakers, cooks, etc. Others we find by taking Wassermans from cases of gonorrhea or other non-luetic patients who deny infection until we explain that their blood is strongly positive, when they admit in most cases having had the disease and having been cured.

We were never able to get any real lasting satisfaction from this large group of cases, but have carried them on with the hope of preventing active tertiary manifestations. We are still anxious to take advantage of the advances in intraventricular and intraspinal therapy and diagnosis, but the facilities are not yet at our disposal.

The Wassermann reaction has not always in this stage of syphilis been a safe indication of the status of the case in hand. Rarely the report is negative during the entire period of observation, but more often a negative or even weakly positive reaction becomes strongly positive during treatment. A full report of our experiences with the provocative action of therapy on the Wassermann is given further on in this paper.

We quote many histories in full to give some idea of the multiplex character of the problem of latent tertiary syphilis. The arrangement of the cases is from most recent secondary syphilis to infection acquired several decades ago. In some instances we will report cases that have received none or very little salvarsan:

REPORT X.—Name, Ch. Age, 24. Date, Jan. 26, 1917.

*Diagnosis*.—Latent tertiary syphilis. Primary lesion, May, 1916. Secondaries, June, 1916. No treatment. Wassermann, June 29, 1916, +++ B. of H. No active lesions.

WASSERMANN	SALVARSAN	MERCURY
Jan. 26, 1917, +++	Jan. to Mar., 1917, 5 doses	Weekly injections
July 10, 1917, +++	Apr. to June, 1917, 1 dose	for five months

Latent tertiary syphilis. The same amount of treatment given in the primary

stage of the infection would have made a lasting impression on the disease. The patient free of lesions knows no need for staying under observation further, and goes his way, a candidate for future trouble.

REPORT XI.—Name, Bo. Age, 53. Date, Aug. 27, 1915.

*Diagnosis.*—Chancre, Aug. 27, 1915. Secondaries, Nov. 8, 1915.

Case observed for one week before secondaries appeared. Treatment with mercury salicylate injections twice weekly for one year when salvarsan begun.

WASSERMANN	SALVARSAN	MERCURY
Nov. 15, 1915, +++	Oct. to Dec., 1916, 4 doses	As above.
Nov. 27, 1916, +++	Jan. to Mar., 1917, 3 doses	None in last
Jan. 9, 1917, ++	Apr. to June, 1917, 4 doses	year because
June 27, 1917, ++	July to Oct., 1917, 7 doses	of pain.
Aug. 7, 1917, neg.		

Unsuccessful therapeutic attack with mercury early in the disease. At beginning of second year when in latent tertiary stage, treatment with salvarsan begun. Negative Wassermann after long course. Provocative tests not yet done. One-third or at most one-half the number of salvarsan injections in the primary stage of the disease would have been many more times as valuable.

REPORT XII.—Name, Ro., P. Age, 28. Date, Oct. 22, 1915.

*Diagnosis.*—Secondary syphilis. Mucous patches and glossitis. Chancre, Feb., 1915.

Treatment: six salvarsans in July, 1916, and mercury for eight months.

WASSERMANN	SALVARSAN
June 10, 1916, ++	Jan. to Mar., 1917, 2 doses
Dec. 19, 1916, +++	Apr. to June, 1917, 1 dose
Mar. 13, 1917, ++	

Sailor comes irregularly when ship is in port. No evidence of syphilitic disease clinically. Treatment begun late in course of lues when spirochete had already found favorable and well-nigh inaccessible resting places.

REPORT XIII.—Name, DeM., P. Age, 28. Date, July 18, 1916.

*Diagnosis.*—Latent tertiary syphilis.

Chancre, Dec., 1915. Secondaries, not observed.

Had 55 mercury injections. No salvarsan.

WASSERMANN	SALVARSAN	MERCURY
Aug. 22, 1916, ++	None	Twice weekly for
Nov. 14, 1916, ++		one year
Jan. 2, 1917, ++		
June 21, 1917, +		

Case treated with mercury alone. After eighteen months patient clinically well but Wassermann +. Provocative test will prove interesting.

REPORT XIV.—Name, LaM., P. Age, 26. Date, June 12, 1917.

*Diagnosis.*—Latent tertiary syphilis. Chancre, Dec., 1915. Secondaries not observed, 20 salvarsan and 20 mercury injections.

Wassermann negative June and Oct., 1916, but +++ in Mar., 1917.

WASSERMANN	SALVARSAN	MERCURY
June 12, 1917, ++	June, 1917, 3 doses	Four injections.
June 19, 1917, ++	July, 1917, 1 dose	
July 31, 1917, neg.		

Instability of Wassermann test after thorough treatment makes one doubt ultimate cure. Focus in viscera, still silent should be watched for. Spinal puncture indicated to rule out nervous system involvement.

REPORT XV.—Name, Ha., L. Age, 20. Date, Jan. 12, 1917.

*Diagnosis.*—Latent tertiary syphilis. Chancre and secondaries, Oct., 1915. Eight months' treatment with pills. 25 mercury injections. One salvarsan. Blood reduced to negative but ++ in December.

WASSERMANN	SALVARSAN	MERCURY
Jan. 12, 1917, +	Jan. to Mar., 1917, 9 doses	Weekly for
Mar. 10, 1917, neg.	Apr. 12, 1917, 1 dose	four
Mar. 13, 1917, neg.	Sept. 14, 1917, provocative	months.
July 13, 1917, neg. No treatment for three months		
Sept. 14, 1917, ++		
Sept. 15, 1917, +++		
Sept. 22, 1917, ++++		
Oct. 10, 1917, ++		

A case clinically cured by mercury and salvarsan. Wassermann negative several times. Provocative action poorly shown, since Wassermann ++ when injection of salvarsan was given.

REPORT XVI.—Name, So., I. Age, 22. Date, Mar. 13, 1917.

*Diagnosis.*—Latent tertiary syphilis. Chancre and secondaries in 1915 untreated.

WASSERMANN	SALVARSAN	MERCURY
Mar. 16, 1917, ++++	Mar., 1917, 1 dose	20 injections
July 31, 1917, +		
Sept. 21, 1917, neg.		

Untreated syphilitic. Marries and gives disease to wife. Comes irregularly and infrequently for mercury, yet Wassermann clears slowly from +++ to + to negative. Provocative salvarsan to be given.

REPORT XVII.—Name, Wa., H. Age, 27. Date, Oct. 20, 1916.

*Diagnosis.*—Latent tertiary syphilis. Chancre and secondaries in 1914. Ten salvarsan and mercury for two years. Wassermann ++ in June, 1916.

WASSERMANN	SALVARSAN	MERCURY
Mar. 6, 1917, ±	Oct. to Dec., 1916, 5 doses	Steadily for
May 4, 1917, neg.	Jan. to Mar., 1917, 4 doses	three months
Oct. 10, 1917, neg.	April to June, 1917, 1 dose	
Oct. 17, 1917, +	Oct. 17, 1917, provocative	
Oct. 18, 1917, neg.		
Oct. 20, 1917, neg.		

Persistent treatment reduces the Wassermann to negative. Provocative salvarsan does not act. Patient has unequal pupils, but no other signs of tabes. Spinal puncture at another clinic was negative.

REPORT XVIII.—Name, Bo., J. Age, 30. Date, Aug. 14, 1917.

*Diagnosis.*—Latent tertiary syphilis. Chancre and secondaries, 1914. Wassermann +++. Three years' treatment. Four negative Wassermans, but +++ on Aug. 7, 1917.

WASSERMANN	SALVARSAN	MERCURY
Aug. 14, 1917, neg.	Aug. to Oct., 1917, 8 doses	Weekly for
Aug. 21, 1917, +++		two months.
Oct. 6, 1917, +		

Example of case considered clinically and serologically cured. Wassermann changes of interest. Patient had alopecia areata. No clinical evidence of lues.

REPORT XIX.—Name, Fi., C. Age, 24. Date, Nov. 10, 1916.

*Diagnosis.*—Latent tertiary syphilis. Chancre and secondaries, 1914. Wassermann +++ Oct. 10, 1916.

WASSERMANN	SALVARSAN	MERCURY
Nov. 14, 1916, +++	Oct. to Dec., 1916, 6 doses	Weekly for
Jan. 5, 1917, +++	Jan. to Mar., 1917, 3 doses	six months.
May 25, 1917, neg.		

Three-year-old case of lues responds serologically to attack of salvarsan and mercury. Clinically there are no symptoms of the disease.

REPORT XX.—Name, McCr., R. Age, 30. Date, Feb. 16, 1917.

*Diagnosis.*—Latent tertiary syphilis. Chancre and secondaries, 1913. One intramuscular salvarsan. One intravenous salvarsan. Mercury salicylate for 1½ years. Wassermann +++, July, 1916.

WASSERMANN	SALVARSAN	MERCURY
Feb. 16, 1917, +++	Jan. to Mar., 1917, 1 dose	Mixed treatment
Aug. 3, 1917, neg.	Apr. to June, 1917, 1 dose	by mouth for
	July to Oct., 1917, 4 doses	6 months.

Unusual response to this amount of salvarsan. The mercury by mouth influences the blood Wassermann more quickly but less permanently in our experience. Provocative salvarsan will be given if patient stays under observation.

REPORT XXI.—Name, Sch., H. Age, 37. Date, Oct. 10, 1916.

*Diagnosis.*—Latent tertiary syphilis. Chancre and secondaries in 1910. 100 mercury injections. 3 salvarsans.

WASSERMANN	SALVARSAN	MERCURY
Oct. 10, 1916, +++	Oct. to Dec., 1916, 9 doses	By injection for
Jan. 9, 1917, +++	Jan. to Mar., 1917, 4 doses	nine months.
Mar. 27, 1917, +++	Apr. to June, 1917, 7 doses	
Aug. 10, 1917, neg.	July to Oct., 1917, 1 dose	
Aug. 24, 1917, neg.		

Clinically no evidence of arterial or cerebral disease. Wassermann persistently positive during treatment, but after four months' rest blood reported negative on two occasions. Provocative salvarsan to be given.

REPORT XXII.—Name, Bl., J. Age, 27. Date, April 27, 1917.

*Diagnosis.*—Latent tertiary syphilis. Chancre and secondaries in 1907. No treatment and no Wassermann tests.

WASSERMANN	SALVARSAN	MERCURY
Apr. 27, 1917, ++		Apr. 27, 1917
May 25, 1917, +		May 25, 1917
Aug. 3, 1917, +		June 15, 1917
		July 3, 1917

Wife's blood negative. Oldest child +++, middle, neg. Infant +++. The radical change in this patient's blood Wassermann with hardly any treatment is one of the stumbling blocks in the prognosis of latent tertiary lues. Clinically there is no evidence of syphilis in man or wife, but the three children are hereditary luetics.

We have seen comparatively few active tertiary lesions. Yet one of the most satisfactory phases of our work has been the intense

satisfaction of the patients as they become well. Especially is this true of the patients whose syphilitic lesion has been improperly diagnosed and for whom nonspecific therapy has been of little avail. Thus, one of our patients, Lo, went about in New York City for eight years helplessly riddled with ulcers and sinuses of supposed tuberculosis, and a subject of both public and private charity. A remarkably small amount of mixed treatment made this wreck of a man presentable and self-supporting.

What place salvarsan has in the treatment of active tertiary cases, we are not definitely able to say. Ulcerative lesions do not disappear within a few minutes as we once fondly believed, but immediate or well-nigh immediate improvement is noted. After several injections, open sores are epithelized over. Mixed treatment has done as well, and the older clinicians have often told us that they saw as rapid improvement with potassium iodide alone before salvarsan was thought of. We believe that salvarsan should be given with the thought of preventing later manifestations of the disease, that in the older days were spoken of as recurrences.

We have not had the good fortune to observe our tertiary cases over a long enough period of time to be able to give an intelligent idea of what happens to the Wassermann reaction under both methods of therapy. Several histories are appended.

REPORT XXIII.—Name, O., J. Age, 50. Date, Oct. 16, 1917.

*Diagnosis.*—Tertiary syphilis. Chancre, 1902. No secondaries. Gumma of each hand, one year duration.

WASSERMANN	SALVARSAN	MERCURY
Oct. 16, 1917, ++++	Oct. to Nov., 1917, 4 doses	5 injections
Nov. 9, 1917, ++++		

Symmetrical gummata over metatarsal bones of both thumbs. No treatment although Wassermann on first appearance of lesions was ++++. Lesions size of silver dollar disappear after four injections. Man able to return to work after enforced idleness.

REPORT XXIV.—Name, Lo. Age, 43. Date, July 22, 1916.

*Diagnosis.*—Tertiary syphilis. Chancre, 1902. No secondaries. Many sinuses over ribs; open wounds on neck and at site of operations for tuberculous (?) glands. Perforation of hard palate.

WASSERMANN	SALVARSAN	MERCURY
July 22, 1916, ++++	Oct. to Dec., 1916, 1	Ten injections and
Jan. 26, 1917, ++++	Jan. to Mar., 1917, 3	mixed treatment.

Patient strenuously and persistently denied any venereal history until told Wassermann +++. Since 1908, had been going from hospital to clinic, from river-side boat to T. B. roof, misdiagnosed T. B. of skin, glands, and bones. Was a pest at every dispensary where his extensive dressings were forced upon the junior and most energetic (as yet) interne or nurse. Routine Wassermann +++. Antiluetic treatment cleared all lesions in two months. Came sporadically for treatment. Mixed treatment by mouth did wonders in this case. Case illustrates the need of keeping lues in mind in any doubtful clinical case.

We hesitate to report our experience with the twelve clinical nervous syphilitics under our care, since we can not give spinal fluid findings. The recent contributions of John A. Fordyce should be reviewed since they embody the meat of the subject. Our meager observations may not be without interest, however. All the cases were clinically positive. Unequal pupils, lid ptosis, crises, shooting pains, changes in the deep reflexes, and trophic ulcers were present. History of infection was given by all except two, and the blood Wassermann in all except one (whose history was positive) was positive. Three of the patients had spinal fluid findings indicative of lues at other institutions. Two of these had had intraspinal salvarsan for several injections, and the third had had one such treatment followed by so great and distressing reaction that he refused more. It is interesting to note that intramuscular mercury gave these patients much more pain than other patients complained of and few of them took their mercury in this form. Mixed treatment did not control the shooting pains or the crises. Salvarsan gave exceedingly gratifying results. The pains were ameliorated or ceased entirely in early tabes. Pupillary signs remained as before, and the patient with right eye ptosis still retained the droop. In one case the patient was able to work in comparative comfort for two or three days after the injection, but was in misery thereafter until the next salvarsan. It was not possible to give him the drug twice weekly, although this was thought of. After long courses of salvarsan, the blood Wassermann became negative in three of our cases, but positive again on resumption of treatment.

The full histories of a few of these cases follow:



REPORT XXV.—Name, Da. Age, 28. Date, Dec. 8, 1916.

*Diagnosis.*—Nervous system syphilis. Chancre and secondaries, 1906. Very little immediate treatment. Recently had 6 salvarsans. Pains of tabes and crises now present.

WASSERMANN	SALVARSAN	MERCURY
Dec. 8, 1916, ++	Oct. to Dec., 1916, 1	Injections gave severe pain.
Feb. 22, 1917. ±	Jan. to Mar., 1917, 10	
June 19, 1917, neg.	Apr. to June, 1917, 1	
Sept. 21, 1917, neg.		

Neglected case of lues, which gives signs of attack on cerebrospinal system. Intravenous therapy reduces a positive Wassermann to negative, but the nervous symptoms are little affected. Requires intraspinal salvarsan.

REPORT XXVI.—Name, He. Age, 62. Date, Nov. 16, 1916.

*Diagnosis.*—Nervous system syphilis. Chancre and secondaries in 1896. Advanced tabes.

WASSERMANN	SALVARSAN	MERCURY
Nov. 16, 1916, +++	Oct. to Dec., 1916, 4	No injections.
Aug. 27, 1917, neg.	June to Mar., 1917, 8	Too much pain.
Sept. 7, 1917, +	July to Oct., 1917, 5	

Advanced destruction of spinal nerve. Pains made work impossible. First salvarsan gave marked flushing of face, but no subjective symptoms. Able to work without pain for two days following salvarsan injection. Spinal therapy indicated, but one attempt give patient agony. Without treatment for six months and Wassermann negative. One dose of drug provoked reaction to + ten days later.

#### CONCLUSIONS

*Primary Syphilis.*—Early syphilis is a curable disease. The demonstration of the spirocheta pallida is proof positive of syphilis, and treatment with salvarsan should be begun at once, and adhered to for a long time to eradicate safely the disease. The period prior to the wide diffusion of the syphilitic virus, that is, the period of chancre, negative Wassermann and no evidence of secondaries, is the primary stage of the disease. This stage is most successfully attacked with intravenous salvarsan. Mercury has not held the invading organism in check. This was the experience of the syphilologists of a decade ago and led them to believe that the chancre appeared only after the defenses of the entire body had been overcome. The converse of this, that the chancre is entirely a local disease, is not true either, since surgical removal of the chancre does not prevent later manifestations of the disease. Early surgical removal of the foreskin in two patients for lesions

not recognized as luetic did not prevent in one instance, enlargement of the draining glands, and in another a generalized macular syphiloderm. Every means in our power should be used in the effort to diagnose chancres early in their course. Clinical skill, and the microscope are both needed. The possibility of intra-urethral and even intrarectal chancres must not be forgotten if there is an unusual discharge from either urethra or anus. The soft chancre should certainly be looked upon with great suspicion. The future of the syphilitic depends on the doctor he first consults. Once diagnosed, the moment for salvarsan treatment has begun in the chancre stage of the disease.

*Silent Generalization Stage.*—The phase of lues next advanced from the primary syphilis is the one to which we have appended "silent generalization stage." The chancre is present, there are clinically no secondary skin or mucous membrane lesions, yet the Wassermann is strongly positive. We conceive of the local glands having been invaded by the syphilitic organism, and from these having entered the general circulation through the medium of the major lymph channels. The spirochetæ pallidæ are free in the blood at this period, but no metastatic foci have had time to evidence themselves. This blood invasion occurs about ten to twenty days after the first evidence of the chancre. Hopes for absolute cure are good, but failure may be expected if the spirochetes find lodgment in a part whose local resistance is below that of the individual, for example in diseased heart muscle. To delay treatment of a suspected syphilitic until the Wassermann is positive is more blameworthy than the older men's motto, "Wait for the secondaries," for they did not have the *treponema pallidum* to demonstrate as we have. Immediate and long-continued treatment should be instituted. Possibility of recurrence is always to be thought of, but we think these far less likely than in the next group of cases with the same amount of treatment.

*Secondary Syphilis.*—We are not as optimistic as most syphilologists as to the ultimate favorable outcome of the frankly secondary syphilitic. The spirochetes have found lodgment in all the tissues of the body, and the defensive perivascular, and perilymphatic infiltration of the host prevent their immediate destruction even by specific medication. Once a syphilitic, always a syphilitic, does not

hold true in the primary stage of the disease; but only lifelong observation of many, many cases will cause us to change the axiom for the clinical secondary syphilitic. The negative blood Wassermann is not a criterion of cure, no matter how often repeated. Spinal fluid findings are necessary. About 25 per cent of secondary luetics who give no clinical evidence of cerebrospinal involvement give positive laboratory indications that nervous syphilis is a matter of time only, and at least another ten per cent of all secondary syphilitics give unmistakable clinical signs in tremor, severe headache, unequal pupils, double vision, or paralyses. Salvarsan and mercury in oft-repeated courses, in spite of the lack of symptoms, should be given. Observation not for one year, or two years, or even five years, but for life will alone prevent, if prevention is possible, the late manifestation of syphilis. Intraspinal therapy by one of the present approved methods is essential in those cases that clinically or by laboratory tests are most exposed to nervous system syphilis.

*Latent Tertiary Syphilis.*—The period following the retrogression of secondary symptoms, either with or without treatment, we speak of as the latent tertiary stage. It is the stage of potentially active syphilis. Generalized eruptions may recur, or isolated lesions manifest themselves as gummata of the skin, bone, or other viscera. Latent tertiary syphilis is most resistant to treatment. The blood serology either remains persistently positive or becomes negative for short periods only. During an intensive course of treatment the Wassermann may be favorably reduced, or the provocative action of therapy may act, and only after the cessation of treatment, does the Wassermann become negative. Resumption of treatment usually provokes the positive reaction. Well-organized foci of spirochetes are present in this stage that neither the natural nor aided forces of the body are able to destroy. Treatment should be maintained periodically as a prophylactic against an uncontrollable outburst. The absence of symptoms may make it difficult to keep the patients under orders, but the importance of treatment should be successfully imparted.

*Active Tertiary Syphilis.*—Except for the involution of active gummata, gummatous infiltration, and poor granulation tissue of broken bones, salvarsan and mercury are of little avail in permanently ridding the active tertiary syphilitic of his infection. The long span of

years that has usually intervened since the acquisition of the infection is an added disadvantage. Possibly mixed treatment is efficacious in removing the accessible lesions, but makes less impression on the silent foci elsewhere that may announce themselves later on. Arsenotherapy should be utilized in the active as well as the latent tertiary luetic with the view of preventing further degenerations. The permanently negative blood Wassermann should be the aim of the therapist, but he must not forget the possibilities of the spinal fluid.

*Nervous System Syphilis.*—In the few cerebrospinal axis syphilitics under our care and observation, intravenous salvarsan gave great relief, and in several cases reduced a positive blood Wassermann to negative, at least temporarily.

## EARLY SYPHILIS AS A PUBLIC HEALTH PROBLEM

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THIS paper is not to be a statistical homily. Neither shall the significance of syphilis to the public be exaggerated nor minimized. The disease, however, is a social threat, the import of which should never be permitted to sink into the background. The human race must constantly be aroused to self-defense against a foe which can be curbed, although at present not exterminated. If there were such a thing possible as premarital asceticism, if monogamy were a fact instead of a delusion, there would be no syphilis. Man, however, being as he is, neither the sermon of the sex moralist, the raving of prudes, nor the sober warnings of those competent to warn, will suddenly alter a custom which tradition has covertly condoned, however greatly indulgence is fraught with danger. Young men will continue to desert the lecture hall of the hygienist for the brothel, and Metchnikoff's makeshift salve will remain a substitute for rational prophylaxis, so long as human nature remains essentially polygamous and polyandrous. Sexual derelictions have been accepted as among the lesser vices and they become a source of repentance only in retrospect when their unfortunate victims labor upon the long,—nay, even endless—road to recovery. Society, though, suffers under a burden directly proportionate to the number so afflicted. Since it is impossible for society to eliminate syphilis, it must face the practical problem of lessening its terrors.

Syphilis, tuberculosis, and cancer are the greatest hygienic problems of humanity. Of these, syphilis is by no means the least. Tuberculosis is largely a matter of environment, and when society sets a value upon human health at least equal to that of a stock dividend, so that poverty will no longer imply squalor and filth, tuber-

culosis will take its place with bubonic plague and variola as a historic disease. Cancer is still nowhere near solution, but unlike tuberculosis and syphilis, it is a condition that at least respects youth and does not strike at humanity during the years of maximum physical and mental effort, or during the years of reproduction, nor is it transmissible. Syphilis, on the other hand, preys upon man during his second and third decades and is the result of impulses accepted as uncontrollable.

There are somewhere between ten and twenty million syphilitics in the United States. If only one per cent of these develop central nervous involvement, there will be one hundred and fifty thousand so afflicted, and this estimate is probably two or three times too low. Nearly all aortic insufficiency and aortic aneurysms originate in syphilis. The number of these cases can not be estimated, nor can it be calculated how many patients suffering with arteriosclerosis, angina pectoris, chronic nephritis, or cirrhosis of the liver owe their diseases to specific origin. Possibly there are two million such cases, or one-fiftieth of our total population. Who can state how many miscarriages are due to syphilis, or how many congenital syphilitics are born annually? If there are only two hundred thousand, this means twenty million in a century. Oriental populations double in this period, while Occidental ones increase by about half this figure, and yet we are not awake to the danger of squandering two-fifths of our procreative ability. The aggregate time lost to society by syphilitics in pursuit of treatment privately or in public institutions is enormous. Assuming that there are only ten million in the United States, that three years are required for the cure, that a half hour is spent in each consultation, and that each patient makes about forty visits annually to his physician, six hundred million hours are lost in this period, or twenty-five million working days a year, or about eighty-four thousand working years. This represents a loss in wealth that can not even be surmised. With the utmost desire for optimism, is not syphilis an adversary worthy of our keenest steel?

As a result of ten years of intensive study, one lesson stands out that is of practical value. The earlier the disease is recognized and treated, the greater the probability of prompt and permanent cure; thus, the likelihood of transmission during the period of maximum infectiveness is decreased, and that of the social sequelæ tends to be

diminished. Society can face its problem either by destroying the disease, or by drawing its fangs. To eliminate the disease, society must become monogamous. To curb the disease, society must take means to safeguard itself by an enlightened, conscientious, concerted, and vigorous series of measures.

The great vehicle of transmission of syphilis is indiscriminate sex congress. In young men the belief is nurtured that continence is injurious. This is absurd, of course, as Haven Emerson recently emphasized in an address before the New York Social Hygiene Society ("How Publicity Can Help to Control Venereal Diseases"). The Germanic tribes of the first centuries of the Christian era held virginity in men as high as in women. If we compare the sexual life of the Northern races to that of the Romans whom they conquered, we can find little to justify belief in the doctrine that continence is harmful either to health or virility.

It is important, then, to combat the superstition that sowing wild oats is a necessary or beneficial activity. Adolescents should be warned by their parents against the physical risks inherent in incontinence. To regard the question as an ethical or moral transgression is another matter. Ethical and moral standards are purely subjective, and sermons and other similar forms of appeal are among the least efficacious means of carrying conviction.

In the last analysis, one may well despair of the likelihood of accomplishing much by addressing individuals. Although every point made may be accepted by a rational human being, everything in society militates against masculine virginity, and the hope of eliminating syphilis by an appeal to reason is slight, although actually this is the only way to attain the end. Society, then, is confronted by a complex problem. Syphilis is an infectious disease of great economic importance, in that it materially lowers the physical and mental quality of the race and, as already indicated, alarmingly lowers the birth rate and the mean average standard of the newborn. A simple expedient exists to meet the condition—sexual continence. The expedient, however, is impracticable since it is at variance with that which in amiable self-delusion we call "human nature." The next best thing to preventing a disease is controlling it. Such control is within the easy reach of society, provided society will assert itself.

Properly trained physicians, properly equipped institutions, and suitable legislation are all that is needed.

The training of capable syphilologists should begin in medical schools. Need for brevity forbids me to trace out in detail my reasons for the views about to be expressed concerning this phase of the question. In another paper I have elaborately analyzed the situation, and here shall simply record my conclusions. A special chair of syphilology and dermatology with faculty representation is required. To divorce the two subjects, since an expert syphilologist must also be an expert dermatologist, would effect a wasteful reduplication in our colleges. The department in question should teach syphilis in its broader aspects, intimately cooperating with all other clinical departments, and with those of pathology and serobacteriology. Suitable clinics should be open to students, and after a two years' course during which undergraduates in medicine have familiarized themselves with the disease in its general and special aspects, they will be ready to take up their postgraduate training. No candidate should get his degree without being able to make a dark-field examination, without having been taught to administer salvarsan and mercury, without understanding the significance of the Wassermann test, or without being able to recognize early syphilis. It is in the early recognition of the disease and in its prompt cure that the hope of the race lies. Shilly-shallying or ignorance where syphilis is concerned are social transgressions on a par with criminal abortion.

The head of the department of syphilology must be a widely trained physician with as broad a grasp of medicine as an internist, and thereunto added great special knowledge. Our medical schools in this connection would do well, when making their appointments to the chair, to emphasize the important requirement of selecting the best possible available man with reference to his ability for his chosen duties, rather than with an eye to his social prestige, or his kinship to an influential benefactor. To make a syphilitic safe for the world rests on principles similar to those involved in making the world safe for democracy, and it would harm American society very little to realize that the dean's college chum, or the nephew of the rich banker who left a million to the university, although a pleasant gentleman, is not necessarily the best choice for the chair of syphilology.



In postgraduate work, as well as undergraduate, the subject should be taught on similar principles in a central department, cooperating intimately with all other departments. Incidentally, postgraduate teaching should be undertaken far more seriously than it is. Mushroom specialists should not be sanctioned, and no man should have the indorsement of a postgraduate school without at least six, and preferably twelve months of intensive training under strict supervision in his elected field. The farmer of the Northwest and the planter of the South are entitled to as good syphilologists as the country can produce, and they should be made to realize that a physician who has vanished from his home for two or three months and who suddenly reappears, posing as an expert, is not necessarily one by virtue of having called daily for his mail at some large metropolitan postgraduate school. Actually, postgraduate teaching to be efficacious, should be supplemented by a year of practical work in clinics and wards, and no physician should treat a case of syphilis unless he can conscientiously tell himself that he would be willing to treat the disease in his own brother.

Whether in postgraduate or undergraduate schools, the subject should be allied with dermatology, because dermatologists have become in general better syphilologists than have men in other fields. This by no means implies either that all dermatologists are good syphilologists, or that all good syphilologists must style themselves dermatologists. The fact remains, however, that to be a good syphilologist an expert understanding of dermatology is required. Syphilis is not a genitourinary disease simply because nearly all cases begin on the penis, any more than it is a throat disease when the chancre appears on the tonsil. Since syphilis has acquired greater scientific interest and its treatment has been invested with greater commercial lure, a powerful effort has been made in various fields of medicine to replace former neglect of the subject by a vociferous if not disinterested step-parentage. This is an actual social danger, for the step-parents regard the quondam stepchild with no unselfish eye, and society is within its rights in examining the qualifications of a physician both as pedagogue and therapist before submitting either to his teaching or ministrations. Practically all of the Class A institutions in the United States, and, so far as I know, all postgraduate schools include syphilis in the department of dermatology. Harvard, the one notable

exception, has a special chair for the subject, the management and leadership of which are above reproach. However, there are two kindred chairs at Harvard, and this obviously is wasteful academically and financially. Sabotage exerted by a disappointed department head against the department teaching syphilis should be suppressed by faculty legislation, for the faculty will realize that medical schools render a public service, one of the chief functions of which is to supply society with individuals competent to combat great scourges. Precisely as the greatest discrimination should be exercised in making an appointment, so if the man selected should prove at any time inadequate for his duties, he should be replaced. The human impulse to make allowances is great, and generosity is never without its appeal; but when leniency constitutes a public risk, the community must suppress all sentimental considerations.

In hospitals and dispensaries the care of syphilitics should be, and throughout the country in fact is, in the hands of dermatologists. The reasons for this parallel those for the need of a central department in our teaching institutions. Salvarsan may be administered, excepting in special instances, in the out-patient service. Such exceptions are cases of central nervous and visceral syphilis as might react unfavorably to therapy with the possible risk of prolonged illness, or even death. The general principles of appointing syphilologists their tenure of service, and the like, should follow along lines similar to those indicated in connection with medical schools. In municipal hospitals the city government determines such matters, and abuses may creep in resulting from political exigencies. In private institutions favoritism may likewise defeat ideal ends. The remedy for this lies in a reconstruction of our views upon the relation between human rights and opportunism. It is clear that party smiles, condescension of trustees, demands of benefactors, should all take a place second to actual ability, if indeed they should be accorded a place at all.

Hospital equipment includes adequate means for therapy, examination, social service work and the like, so that early syphilitics may as rapidly as possible, by intelligent treatment, cease to menace the public. A part of this scheme embraces efficient following up by the social service bureau in order that recalcitrant patients may be urged to receive sufficient treatment, until the laws of the com-

munity are able to coerce them. It may become necessary for the community to pay hospital physicians for their work, or even to conduct the work under municipal supervision. There is unquestionably, however, still enough public spiritedness among physicians to enable society to obtain the services it needs without compulsion. Often those most devoted to public welfare are discovered among the busiest physicians, and there is scarcely a man who, within ten years of his graduation, has not sufficient leisure to contribute substantially of his time for the common weal.

Legislation directed to the control of syphilis may have to include measures regulating its teaching and treatment. It is to be hoped, however, that this sort of communistic authority will never have to be exerted in our country. Socialism is perhaps an expression of inability on the part of a race to live up to those humanitarian ideals that should be obvious to civilized man. It is an attempt to enforce the principle of the greatest good to the greatest number. In handling the problem of syphilis this means the State's right to exact proper treatment by properly trained physicians,—factors which depend upon properly conducted medical schools, clinics and hospitals. Unless physicians and trustees are willing unselfishly to accept this basis for their work, society will ultimately enforce its rights and resort to conscription and compulsion.

Aside from legislation directed to the above ends, another great phase of the situation may be met by this means—social prophylaxis to counteract the failure of individual prophylaxis. In other words, the syphilitic, while infectious, must be virtually isolated. How to accomplish this is a matter involving at once delicacy and firmness. The main weapon will be the reporting of cases, both in institutional and private practice, as outlined by Haven Emerson in the paper already quoted.

Naturally, syphilitics will shrink from being enrolled on public records. Society's absurd stigmatization of the unfortunate, and the fear of blackmail by unscrupulous officials, will be the basis of opposition to such a statute, and the fact that among men of prominence in all walks of life are many syphilitics will further fortify such opposition. The reporting of the cases alone would be valueless were society, through proper officers, unable to insist upon adequate care. Thus, laws would have to be enacted forcing patients

to receive treatment, either institutionally or privately, and to have reports of progress filed at stipulated intervals, say quarterly, with the local health bureau. If for some reason the patient should have to change his place of treatment, or his private physician, the successor should be entitled to the records of the predecessor; in fact, the two should be compelled to make the records continuous. The predecessor should report to the health board the patient's discontinuance of treatment, and the successor should immediately announce the arrival of the patient. The names of all the patient's physicians and a record of his treatment should be on file with the health officers. Marriage licenses should be granted only with the consent of the health department. The health departments in various municipalities would have to work in harmony in order that syphilitics might not escape their obligations to the public by leaving one community and joining another. This might, and probably would, involve the creation of a federal department of health with jurisdiction over all local bureaus. Since the American public prefers to close its eyes to prostitution rather than to regulate it, the medical control of prostitutes can be attained only by reporting syphilitics without inquiring into the habits of life determining the infection. Our societies for the suppression of vice still are conducted on the principle that the best way to eliminate the Devil is to tire him out by driving him from one part of a city to another. That the Devil has better endurance than his pursuers never has dawned upon the latter, and the risk of disseminating foci of venereal infection by scattering brothels appears more virtuous to the virtuous than to control prostitution, and examine and license the prostitutes. By reporting all cases of syphilis, those developing among prostitutes will automatically be recorded and cured, and society will be able to continue to blind itself to the existence of the ancient institution and at the same time protect itself.

The federal health bureau should exclude aliens with any symptom of syphilis, even with only a Wassermann reaction. Such a measure will be necessary after the war, when immigration resumes its former proportions, for syphilis has increased enormously in Europe. In the Port of New York the execution of such a law would involve tremendous labor, but it would be worth the effort

and cost to the country, and if syphilitics were deported at the expense of steamship lines, it is safe to predict that these would see to it promptly that no syphilitic embarked for American shores. This would probably lead to universal control of the disease, in the manner outlined, as no nation would care to boast of having an unduly great syphilitic population.

To sum up in a few final words, syphilis is as easily preventable as any other infectious disease. It can not be prevented by an appeal to individual reason, for man has counted the cost, and his knowledge has never frightened him into continence. With syphilis as an actual condition, it must be treated early if its economic consequences are to be averted. Thus the problem of syphilis to the community resolves itself into the problem of controlling early syphilis. This is the period of maximum transmissibility. The disease can be combated only by recognizing it and treating it intensively at once. This places the burden squarely where it should be,—upon medical schools, hospitals, and clinics. These institutions must rise to the occasion by acquiring competent teachers, physicians, and equipment. The department of syphilis must be centralized. Social service bureaus must be adequately conducted, the cases must be reported to the municipality whether by institutions or private practitioners, and finally, alien syphilitics must be excluded at our borders.

## EPOCH-MAKING CONTRIBUTIONS TO THE STUDY OF SYPHILIS

### II. PHILIPPE RICORD

#### Inoculation Experiment\*

**W**ELL convinced that the subject was not exhausted, and that I had another mission to fulfill; encouraged by the most celebrated names and the greatest authorities, I commenced the researches, the results of which I am now about to relate.

It has been asserted, that the venereal virus is a chimerical and intangible essence; that the effects imputed to this imaginary cause only depend upon the nature of the seat, the peculiar vitality of the diseased parts, the different degrees of inflammation, and the sympathetic reactions which may result from it.

I had, therefore, to endeavor to materialize this cause, to coerce this pretended imaginary essence, assign it definite and specific characters, which should not allow it to be mistaken, but by ignorant and uncandid persons; and to prove that the seat, vitality, and functions of the organ, have only a secondary influence upon it, and that it was not the more or less fortuitous consequence of inflammation.

If we are to study a body, and distinguish it from those with which it may be confounded, must it differ from them in every point? Are all the characters of each order, genus, and species different in physics, chemistry, or natural history? Is not one often sufficient to distinguish the difference? In our medicinal substances, for example, is it always easy to point out the essential condition which gives a substance a property, not possessed by another, which is nevertheless in many respects analogous to it? And does this property although invisible, immaterial, and not separated from the substance which possesses it, constitute an entity? Undoubtedly not. The incontestable existence of the venereal virus is proved by a peculiar property of a distinct morbid

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\*A Practical Treatise on Venereal Diseases, Philippe Ricord, translated by Drummond, Philadelphia, 1843.



Philippe Ricord (1799-1889).





secretion, and therefore the pus furnished by certain syphilitical affections has the constant and regular property of reproducing a pus similar to itself, by an action similar to that which first secreted it. We may, by this essential character, distinguish from each other different animal physiological and morbid secretions, with the same precision as we do chemical substances. If we inoculate the venom of the viper, the saliva of a mad dog, the pus of variola, vaccine or syphilis, we shall have specific effects, which will leave no doubt of the difference and peculiarity of the causes which produced them.

Syphilitic pus may present globules more or less resembling those of other kinds of pus. It may, according to the locality, be combined with other morbid or normal secretions, particularly with mucus in form of muco-pus. According to the locality or its combinations, it may remain alkaline or become acid, it may contain animalculi or be devoid of them; but, as distinguishing and specific character, it can inoculate itself and produce characteristic results.

Convinced, nevertheless, as I have before said, that syphilis is one of the most serious diseases which can afflict mankind, I was obliged to exercise the greatest prudence and reserve in my researches, yet without being deterred by pusillanimous fears. I still feel convinced, that it is not allowable for a surgeon, under any pretext whatever, to communicate to a healthy individual a disease, the consequences of which can not be foreseen; and if in consideration of the interest of science, which undoubtedly influenced them, we might find some excuse for those who have thus experimented, their example can not now be followed without culpability.

Although the experiments upon animals were negative in their results, even in the hands of the most experienced men, I felt it necessary to repeat them. Public experiments have been made in my clinic, at the *Hopital des Veneriens*, upon dogs, rabbits, guinea pigs, cats, and pigeons, and in all cases with negative results.

All the experiments repeated in every possible way of infection and inoculation, without neglecting any necessary precautions, were each time made with pus, which at the same time produced in man positive results; so that after these experiments, joined to those which we already possessed, we may conclude that the inoculable principle of syphilis is peculiar to man, and can not be trans-

mitted to brutes. This, however, as we have seen, does not prevent them from being subject, under the influence of irritating causes, to inflammations of the sexual organs, which, as in all other tissues, may be followed by suppurations, ulcerations, etc., without these lesions being connected with the syphilis of man.

Let it however, be remembered, that even if anyone should be able to transmit true syphilis to an animal, that would not detract anything from the specific nature of the syphilitic principle, any more than the possibility of transmitting the vaccine of the cow to man, disproves the peculiar nature of this virus.

Hitherto, then, syphilis can only be inoculated in man; but, as we said above not being allowed to pursue the researches from a diseased to a healthy individual, my observations were necessarily confined to the patient himself, they were founded upon the following propositions:

1. A venereal affection already cured, or still existing in whatever period it may be, does not prevent others being contracted, and the number of possible successive infections are without limit.

2. No individual actually infected and under the influence only of primary symptoms in one region, ever sees symptoms similar to the first developed in other parts of his system, except by a new contagion from contact with the pus of the first, or communicated by another individual.

3. Secondary symptoms, or general infection, never prevent the patient from contracting other primary.

4. The frequency of constitutional syphilis is in nowise dependent on the number of primary symptoms developed at one time.

Do not the observations of former times unite with every-day experience, to corroborate the experiments of Hunter, which prove that one infection does not prevent a second; not only in the development of symptoms different in form and principle, but also of those which are owing to a cause of the same nature? Do we not continually see patients who have a gonorrhea contract a chancre in a fresh sexual intercourse; or having at first a chancre are attacked with gonorrhea, after a fresh coition? I should think no candid person would attempt to deny so well known a fact. But the manner of the production of every symptom which follows the first, might be congested. Those who think there can not be a primary infection without gen-

eral symptoms, look upon all those which follow as in consequence of a first symptom, without the necessity of a new contagion. Thus they attribute distinct diseases, contracted at different times, to the same cause. But it must be evident to all accurate observers who will take the trouble to distinguish primary from secondary symptoms, that the primary can only be produced by the direct application of the contagious pus to the part, or by the conveyance of this pus by the *vasæ lymphaticæ efferentes* to the ganglions in which they terminate, without ever passing them.

The experiments I have made on this subject are very numerous, and to verify them at any time, it will suffice to know the intention in which they were made.

It is thus that in all individuals affected with primary reputed venereal symptoms of all kinds, artificial wounds, or operations performed at a distance from the venereal lesions have never assumed the syphilitic appearance, nor any of the characters of venereal affections, when proper precautions have been taken to prevent their being soiled by the contagious pus. Many examples have been cited, of wounds having assumed the character of primary ulcers, evenomed by the general infection, and nothing is said to be more common in leech bites. Yet in all these cases where the real explanation was overlooked, the true cause might have been found. Thus we often see, where a number of leeches have been applied on and around the penis, some of the wounds assume the appearance of chancre, whilst others heal at once. If we search for the cause of this difference in wounds of similar nature in the same region, we shall soon see that those alone are attacked with which the penis could come in contact, whilst those which are out of reach remain uninjured. A woman in one of my wards, at the *Hopital des Veneriens*, had a number of chancres on the vulva; these chancres were primary, and at the period of development they furnished an abundant suppuration, when she was seized with a rheumatic pain in the right malleolus exturnus, to which some leeches were applied. Some days after, the patient who had at first been much relieved by the leeches, complained that the bites were very painful; she was examined, and they appeared inflamed and like pustules of *ecthyma*, to which succeeded ulcers, having all the characters admitted to belong to true chancre. The part where the

leeches had been applied, the distance of the situation of the primary ulcers of the vulva sufficed for most of the gentlemen who attended my clinic, to regard this accident as a consequence of a general infection, or a bad disposition in the subject. I ordered some more leeches to be applied to the other leg and also some fresh ones to the same leg, taking care to prevent any consequence to these new wounds by isolating them from all contagious contact; and then whilst two punctures made with a lancet, one with the pus taken from the chancre of the vulva, and the other from the ulcerated leech bites, produced ulcers like those which furnished the pus, the wounds which had been guarded from soil healed without any accident.

But it sometimes happens that leeches, applied to bubos cause ulcerations of a malignant nature, without the origin being traced to the application of contagious pus. In these cases, either the leech bites are simply irritated or inflamed, and have been followed, as it often happens, by a kind of furuncle which suppurates, and then the pus which they furnish does not inoculate; or having become true inoculable chancres, the infection was communicated from within, outwards, i. e., that being placed upon a virulent suppurated bubo, the pus of the ganglionic chancre has inoculated the leech bites in passing them, to make its escape. This is the same with every analagous wound, whether accidental or artificial.

Fabricius Hildanus relates, that a man affected with the itch, was in 1609, infected with syphilis, of which he died from having slept in sheets in which several syphilitic persons had sweated. But he has omitted to state in what condition these latter were, and whether they had any ulcers. It is more than probable that some such affections existed, and that the pus which flowed from them, having adhered to the sheets, afterwards came in contact with some points of the skin which were deprived of the epidermis.

I have stated, as has been proved by experiment, that the cessation or persistence of a primary symptom, in whatever period of its existence it may be, does not prevent the patient from being susceptible of contracting another. But the most important point and which alone would authorize us to pursue our researches, sanctioned as it is by Messrs. Fricke, of Hamburg, Lallemand, of Montpellier, Ruef, of Strasburg, and Blandin, surgeon of the Hotel Dieu, of

Paris, etc., is that the number of secondary symptoms stand in no relation to that of the primary symptoms developed at one time. That there are not more symptoms of general infection after two, three, four or five chancres, contracted at the same time, than after a single one, is proved by observations during six years, and can not now be doubted.

These facts being once established, I reviewed all the reputed venereal affections, whether primary or secondary. All the normal or morbid secretions of persons reputedly syphilitic, have been examined by means of inoculation, and only one form has given uniform and constant results, and this form is the primary ulcer or chancre, which is to constitutional syphilis what the bite of a mad dog is to hydrophobia, does not nevertheless produce a specific pus, but at a certain period of its existence; and it is evident that it is from not having paid attention to this simple fact, that the results of inoculation have been contested or appear uncertain.

The primary syphilitic ulcer can not always be the same in all its stages, and it can not cicatrize without first becoming a simple ulcer by the destruction of the cause which served to maintain it. Similar characters and results can not be required from these different phases; it is in the period of development or statu quo of the ulceration, whilst there is no effort of cicatrization that a chancre secretes the venereal virus.

The specific nature of the secretion of chancre, as we have often before said, does not depend upon the organ affected, nor the vitality, functions, or sympathetic reaction of this organ, nor upon the degree of inflammation which may attend the ulceration.

The locality has so little influence upon the peculiar nature of chancre that it can not justly be regarded as proper to the sexual organs. Indeed there is no part of the skin which may not become the seat of it; no part in the necessary condition and being accessible is secure from it. If it be developed on other regions than the sexual organs, it yet maintains, without exception, all its characteristic marks.

Thus a chancre on the end of a finger, on the thigh, foot or the tip of the tongue, will, if it has not been modified, produce pus capable of producing a similar chancre by inoculation, without the participation of the sexual organs; whilst no other affection of these organs,

whatever its form or extent, or the degree of inflammation which may accompany it, can reproduce a chancre.

One circumstance, however, is undoubtedly true, and may have induced the error; viz., that the sexual organs are most frequently affected, like certain bones, which, from their texture and situation, are more frequently fractured than others. The delicate tissues of these organs, the facility of erosion of the epidermis or epithelium, the number and exposure of their follicles, the intimate and prolonged connection they maintain between a healthy and a diseased individual, are the conditions which permit the cause also to act with so much more effect. But, as experience proves, it is the organ that gives to the disease its peculiar and specific nature; for no artificial lesion, whatever the agent employed may be, can produce it; and whilst a finger deprived of epidermis, contracts a chancre by contact with the pus, the sexual organs being entire in every point, may be soiled with it unharmed.

Thus we have established this fact, that chancre, whatever its seat, is the consequence of a specific pus, which it alone secretes, and which justly termed, true leven (veritable levain, ferment special) reproduces an identic disease wherever it is suitably deposited.

But this peculiar leven, which has only a peculiar action when it produces an ulceration, is only generated during a certain period of a chancre, which, as we have seen, has two very distinct stages. The first, to which the name peculiarly belongs, is that of increasing or stationary ulceration, this is the one which furnishes the specific pus; at the second, which is the stage of reparation, it can only arrive by first becoming a simple ulcer; this is capable of cicatrizing, and no longer furnishes the specific virulent secretion.

The importance of the distinction of these two periods of chancres will easily be seen, for without it all is confusion; and the same ulceration which produced a chancre by inoculation, not yielding contagious pus a few days later, one would conclude the experiments to be uncertain, where, in fact, they are of the greatest value.

If a little of the matter secreted by a chancre, during the period which we have pointed out, be taken upon the point of a lancet, and inserted under the epidermis, we shall find the following result:

During the first twenty-four hours the punctured point becomes red, as in vaccination; the second to the third day, there is a slight

swelling, and it has the appearance of a small papula surrounded by a red halo; the third to the fourth day the epidermis, elevated by a more or less turbid fluid, often assumes a vesicular form, with a black point on the summit, caused by the drying of the blood of the little puncture; the fourth to the fifth day, the morbid secretion increases, becomes purulent, the pustular form is more defined, and its summit becoming more depressed, gives it an umbilicated appearance, which makes it resemble the pustule of the smallpox. At this period the aureola, which has increased in extent and intensity, begins to vanish or diminish; but from the fifth day, the subjacent tissues which have often hitherto remained unaffected, or were slightly edematous, become infiltrated and hardened by the effusion of plastic lymph, which gives to the touch a sensation of resistance and elasticity, like certain cartilages; lastly, from the sixth day, the pus becomes more thick, the pustule cracks, and crusts soon begin to form. If these are not detached, they increase at their base, and rising in layers, assume the form of an imperfect cone, with a depressed summit. If these crusts be detached, we find beneath an ulcer which being seated on the hard base we have mentioned, presents a ground whose depth is equal to the entire thickness of the skin, and whose greyish surface is formed of a fatty substance, or sometimes a pseudomembrane, which can not easily be detached. The edges of the ulcer at this period cleanly cut, as if by a perfectly circular punch, are yet undermined to a greater or less extent, and viewed with a lens, present slight indentures, and a surface similar to that of the ground; their margin, the seat of a similar engorgement and induration as the base, presents a kind of red-brown, or more or less violet circle, which more projecting than the neighboring parts, raises the edges and reverses them a little, which in the first period gives a funnel-like appearance to these ulcerations.

These regular and constant signs, which form a general rule, the rare exceptions to which are easily explained, lead to the following propositions:

1. A chancre is not to be recognized, *a priori*, in all cases, either by its virulence or because it was contracted in a suspicious coition, or from its seat, the induration of its base, its color, the consistency of the ground, the cut, undermined or callous edges or the tint of its margin, but by the pus which it secretes, and the vitiation of the sys-

tem to which it may give rise, as all the above mentioned conditions may vary, the secretion, and its general consecutive effects, remaining alone the same.

2. The pus of a chancre alone produces a chancre.

3. The best method of producing a chancre is by inoculation with a lancet.

4. To produce a chancre, neither the orgasm of the venereal act, nor previous excitation of the part about to be inoculated, is necessary.

5. Inoculation never fails if the pus be taken in the proper state and well applied.

6. The pus taken from a pustule, produced by inoculation, reproduces a chancre in the same manner, and so on from one to another, without limit.

7. If several punctures be carefully made with pus from the same ulcer, each produces a pustule, and then a chancre.

8. The pustule and the chancre which succeed it, are developed upon the precise point of inoculation.

9. Whatever varieties and complications the chancre from inoculation may present at a later period, its progress in the commencement is always the same as we have just described; the pustulous period is wanting only when the infected parts are denuded of epidermis, and it is only preceded by inflammation and abscess when the virulent matter has been introduced into the subcutaneous cellular tissue or the lymphatics.

10. There is no incubation in the sense in which this word is generally used; for the evolution of the chancre commences at the moment of contact with the infecting pus, and continues till the formation of the ulcer.

11. Chancre is at first a local disease.

12. The symptoms of general infection, which can only occur when preceded by chancre, never appear when they do occur, except it has lasted a certain period.

13. To arrive at this important result, we must distinguish the real from the apparent commencement of the chancre; viz., not reckoning from the day on which the patient first perceived it, but from the time of infection.

14. In making observations for this purpose, it will be found that



ulcers, completely destroyed by caustic or otherwise, in the first three, four or five days subsequent to the application of the cause, do not expose the patient to secondary inflammation.

15. The induration of chancres only begins about the fifth day. Mostly they are indurated chancres which are followed by secondary symptoms, and this induration would seem to indicate that the venereal principle has penetrated the system, and as long as it does not take place, we may conclude that the disease is superficial.

It appeared to me very important to ascertain whether the specific matter produced by chancre, preserved its contagious properties for a certain time, like vaccine. Numerous observations, and amongst others, those of Hunter, one would think no doubt left upon this subject; but this, however, is not the case, as we see by what the late Cullerier says upon it, in the great *Dictionnaire des Sciences Medicales*.

# Abstract of Current Syphilis Literature

It is the purpose of this JOURNAL to review so far as possible all literature on syphilis as it appears in other medical periodicals and to present it in abstract form. Authors are requested to send abstracts or reprints of their papers to the Associate Editor, Dr. Wm. H. Deaderick, Dugan-Stuart Bldg., Hot Springs, Arkansas.

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WM. H. DEADERICK, M.D., EDITOR

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SECONDARY SYPHILIS IN THE INDIGENOUS MUSSELMAN OF NORTHERN AFRICA.—Montpellier, Algiers. *Annales des maladies veneriennes*, 1917, vol. xii, p. 732.

Secondary syphilis in the Mohammedan of Northern Africa does not differ from the same affection in the European. The cutaneous and mucous membrane manifestations show no differences in respect to number, precocity, etc. At most one might think of a greater tendency of the cutaneous manifestations to ulcerate, but this has not been demonstrated. Years of experience in the center for venereology in Algiers have enabled the author to go on record strongly as to the verity of his claims.

THE PATHOLOGICAL FINDINGS IN THREE CASES OF JUVENILE GENERAL PARALYSIS.—Charles Ricksher, Kankakee, Illinois. *The Alienist and Neurologist*, 1918, vol. xxxix, p. 16.

The pathologic changes may be summarized as follows: Thickening of the pia, often rather extreme, with infiltration with lymphoid and plasma cells. In some cases the lymphoid cells are extremely numerous. The cortex shows various atropic areas and there is usually considerable atrophy of the convolutions with widening of the sulci and a compensatory subpial edema. The cerebrospinal fluid is usually increased in amount, and the ventricles may be somewhat dilated even up to a real hydrocephalus. The nerve cells are diminished in number, especially from the outer layers inward, although the opposite has been recorded. The nerve fibers in the cortex, especially the tangential fibers, are destroyed, and the radial fibers suffer more or less in the various cases. The neuroglia cells are very much increased in number and in size. The neuroglia fibers form a thick network under the pia and are more or less pro-

nounced throughout the cortex. The blood vessels show a marked increase in number and large numbers of new-formed blood vessels are found and many of the endothelial cells show various proliferative changes, such as budding processes, and in some instances, mitotic figures. About the blood vessels there is a layer of lymphoid and plasma cells as in adult paresis. The plasma cells, however, usually predominate. Mast cells are not especially numerous. Developmental defects, such as embryonic type of cells in the cortex and especially in the cerebellum, are usually found. In the basal ganglia there may be atrophy, suggesting developmental defects, or areas of softening and the medulla frequently shows changes in form due to atrophy or developmental faults.

CHANCRE OF THE EYELID.—Philip F. Shaffner, Chicago. *Journal of the American Medical Association*, 1918, vol. lxx, p. 676.

A widow, aged fifty-eight, Irish, consulted the author for a lesion of four weeks' duration, situated on the left lower eyelid. In addition to the ulceration on the lid, a large, painless, hard, freely moving gland could be palpated under the angle of the left jaw. A clinical diagnosis of primary syphilis, which was confirmed by the spirochete pallida with the dark-field illuminator, was made. After prolonged questioning of the patient as to the possible mode of infection, it was learned that a member of her family had had a "sore throat" for some months. Examination of that person revealed a typical syphilitic angina, mucous plaques on the cheek, a fading roseola and a generalized lymphadenopathy. This patient finally volunteered the information that she had employed the tongue to remove a foreign body from the victim's eye. This was unquestionably the mode of transmitting the infection to the eyelid. Extragenital lesions of the eye are extremely rare, and the ratio of incidence is 1:67. They occur mostly in physicians, usually through patients coughing contaminated saliva into their eyes. This brings up the interesting fact that a single lesion in the mouth may contaminate the saliva to such an extent that a drop of the contaminated saliva may produce a syphilitic lesion without the lesion of the donor coming in actual contact with the recipient of the disease.

SYPHILITIC ORIGIN OF VITILIGO.—Merklen. *Journal de Medicine de Paris*, 1918, vol. xxxvii, p. 15.

Not long before the war several physicians reported cases of vitiligo with positive Wassermann reaction. This was the more remarkable because the older syphilographers had never mentioned such an association. The author has recently had occasion to test two subjects with vitiligo from this viewpoint. The first patient had chronic aortitis and vitiligo of extensive distribution. There were, however,

no further clinical evidences of syphilis and the Wassermann was negative. On the other hand, the second subject who had had a generalized vitiligo for ten years and had also chronic aortitis, gave a positive seroreaction, although he seemed clinically as free from syphilis as the first man. On account of the association vitiligo-aortitis there must be a suspicion of the specific origin, despite negative seroreaction in Case I. Leblanc's case of syphilitic vitiligo showed also one other probable symptom of syphilis; to wit, rigid pupil.

SYPHILIS OF THE PANCREAS.—Udaondo. *Revista de la Asociacion Medica Argentina*, 1917, vol. xxvii, p. 19.

The author reports a case without autopsy or operation in a man aged 47 with neither history nor evidence of syphilis, who had complained for some weeks of pain in the epigastrium, loss of flesh, and diarrhea. A careful examination led to the diagnosis of achylia pancreatica. Under special diet with pepsin-HCl he showed no improvement, and pancreatic preparations caused but slight transitory benefit. The achylia was thought to be due to pancreatitis and the occurrence of an abortion in the wife during the treatment led to the taking of a Wassermann, with positive outcome. The bichloride of mercury was at once injected into a vein and after the fifth injection the symptoms began to clear up. Several months after relative recovery, the pancreatic functions were tested anew and found to be notably improved. The patient had regained much of his lost weight.

UTERINE SYPHILIS.—J. Bordarampe. *Revista de la Asociacion Medica*, 1917, vol. xxvii, p. 417.

One case is reported in a woman of forty-eight years. Her menstrual life had been normal. Married at twenty-eight, she had been pregnant three times. The firstborn died within its first year, and patient next gave birth to twins. She aborted once at thirty-eight. Two years before admission to the clinic she began to suffer from attacks of metrorrhagia, which masked her menstrual periods. Treatment was not sought until after a profuse flowing, which lasted six days. The hemorrhages alternated with profuse hydrorrhea. When first seen she was anemic and run down. The uterus corresponded in size to that of ten weeks of pregnancy. Aside from some prolapse from ruptured perineum, the pelvic organs were otherwise normal. The cavum uteri, which was 10 cm. deep, was curetted, chiefly for diagnosis. Biopsy showed a thickened degenerated mucosa. In the course of a systematic general examination the Wassermann was found to be positive. A much more careful biopsy was now made, excluding malignancy. The mucosa appeared to have been the seat of an inflammatory-sclerotic process involving the

vessels. As the hemorrhages disappeared promptly after a few intravenous injections of bichloride of mercury and KI, this process was assumed to have been syphilitic.

**A CASE OF SYPHILITIC POLYNEURITIS.**—E. M. Villapadierna, Madrid. *El Siglo Medico*, 1917, vol. lxiv, p. 906.

The patient, a woman, was thirty-six years old. Beginning as a child, she had worked for years in the lead mines. At the age of fifteen she became the common law wife of a miner. The period of infection was unknown. Aside from several abortions, her health had always been good. She had one living child eleven years old. The neuritis began three years ago with pains in the limbs and difficulty in walking. At the same time an ulcer developed in the ischial region, suggesting the causation of the neuritis. Injections of mercury were without benefit. When seen by the author, she still had deep ulcerations with flaccid paralysis of the limbs, and muscular atrophy with contractures of the toes. There were marked sensory disturbances. A lumbar puncture appeared to show that the cord was not affected. The diagnosis lay between lead neuritis and syphilis. The Wassermann reaction was positive. There was, however, a history of probable lead colic. The author expects to arrest the affection with salvarsan, but owing to the chronic condition of the malady, and the contractures, the result will be neither prompt nor complete.

**HERPES ZOSTER SYPHILITICUS.**—Boner. These de Paris, 1917. (Abstract in *Journal de médecine et de chirurgie pratiques*, 1917, vol. lxxxviii.

Syphilis is known to play an important role among the causal elements of herpes zoster. The spirochete has been shown to attack the ganglion of the spinal nerve roots and this lesion may accompany other manifestations of syphilis, such as early meningitis. Moreover, zoster may be a close forerunner of paresis and locomotor ataxia, as well as of syphilitic epilepsy. Zoster in an old latent syphilis may indicate an active recrudescence of the disease. This has been seen in old chronic meningitis. It is evident that there is some relationship between zoster and a meningeal localization of syphilis; or, speaking more broadly, there is some factor in common in radiculitis, pachymeningitis, encephalitis, myelitis, etc.

**A CASE OF COMPLETE SYPHILITIC ALOPECIA.**—George C. Kindley, Dallas, Texas. *Journal of the American Medical Association*, 1918, vol. lxx, p. 86.

A section laborer, white, single, aged forty-nine, examined April 8, 1915, complained of slight cough and some pain in right side of

the chest. The family history was negative, and venereal disease was denied. He had smallpox two months previously. The patient was of ordinary stature and weight and was fairly well nourished. The head was perfectly bald. There were no eyelashes, no whiskers, and no axillary or pubic hair; in fact, not a hair could be found anywhere on his body. The back of his neck had a pink appearance. The deep reflexes were considerably diminished, but there were no pupillary changes and no ataxia. His own story was substantially as follows: Four years previously he had begun to work for the Santa Fe Railway near Lometa, Texas, handling creosoted ties. He had work at this job for two years, during which time his hair had come out a little in places, and yellowish spots had appeared on the back of his hands and neck. One year after he had stopped handling ties, that is, in June, 1914, his hair had begun to fall out, and in two months it was all gone. He could rub the skin off his hands and neck, so the yellow spots had disappeared in this way. He had thought it was all due to heat; but when a lawyer told him it was caused by the creosote, he had decided that at some future time he would sue the railroad. The Wassermann test was found to be strongly positive. Patient refused antisypilitic treatment, and in a few days left the hospital. He subsequently sued the Santa Fe Railway for \$20,000 damages. At this time the deep reflexes were purposely inhibited or exaggerated. His gait was somewhat ataxic and he had a marked Romberg. The pupils were distinctly sluggish to light and only slightly responsive to distance. The jury returned a verdict in favor of the defendant.

FACTS CONCERNING ALOPECIA AREATA IN HEREDOSYPHILITICS.—R. Sabourand, Paris. *Presse médicale*, 1917, vol. xxv, p. 660.

The author reports 16 cases of alopecia areata in subjects with probable hereditary syphilis. Evidences of the latter were largely dental, with special reference to the coexistence of a well-developed Carabelli's tubercle. The latter is described as a nipple-like prominence on the internal aspect of the first upper molars. The dentists have denied that this anomaly is a dental stigma of syphilis, but the author reasserts his original claim that when highly developed it is *per se* evidence of the inherited disease. The general relationship between anomalies of dentition and shedding of the hair was worked out by the late Jacquet. A survey of the author's cases appears to show that the alopecia was of a recurrent type, with a tendency to extend to the eyebrows, and to some extent, to all the hairy surfaces. In some of his earlier work in this field, the author did not practice serodiagnosis, but in the present material the omission has been partially made good.

**SYPHILIS OF THE PROSTATE.**—Portillo. *Revista española de urologia y dermatologia*, 1917, vol. xix. p. 620.

The author's case appears in the proceedings of the IV Congress of the Spanish Urological Association. The patient presented himself with orchitis and diurnal and nocturnal pollakiuria. There was a history of chancre and mucous papules. The testicular lesion was recognized as syphilitic sarcocele, bilateral. The urethra was normal. The rectal touch discovered a prostate with its right lobe greatly enlarged, firm and insensitive. A diagnosis was made of sclerous syphilis of the prostate. After eleven months of vigorous and continuous antisyphilitic treatment the case ended in recovery. In discussion Bartrina stated that he had seen a case of syphilis of the prostate in a tabetic. As fluctuation was present, the case was treated surgically by the perineal route, its nature having been overlooked. No improvement resulted until the patient was placed on an antisyphilitic regimen, when recovery followed.

**SYPHILIS AS A CAUSE OF DIABETES MELLITUS.**—John R. Williams. Rochester, N. Y. *Journal of the American Medical Association*, 1918, vol. lxx, p. 365.

Many combined clinical and pathologic studies reported in the literature support the belief that the Wassermann reaction as a clinical diagnostic aid is a dependable procedure in from 70 to 90 per cent of all types of syphilis. In the hands of clinicians who have had a wide experience in the study of diabetes, the Wassermann test has been positive in only from 3 to 10 per cent of the cases examined. In my experience, only four cases out of 143 examined thus reacted. Careful physical examination of 126 cases for the lesions which characterize syphilis does not lend support to the view that the disease is a common causal factor in the production of diabetes. Thirty-seven of the author's patients had a cholesterinemia and yet reacted negatively to the Wassermann test. Since cholesterol is purposely added by serologists to increase the delicacy of the test, it would seem that if these patients had had the slightest trace of syphilitic infection, they would have reacted positively. This study does not support the view advanced by Warthin that syphilis is the chief etiologic factor in the production of pancreatic diabetes. Indeed, if it proves anything, it is that syphilis is rarely the provocative agent.

**SYPHILIS OF THE EYE.**—William Campbell Posey, Philadelphia. *New York State Journal of Medicine*, 1918, vol. xviii, p. 50.

That the administration of salvarsan does not prevent the appearance of new syphilitic symptoms during the period of administration is generally recognized and is probably due, as Stephenson

has pointed out, to the presence of nests of organisms which escaped the action of the initial dose. Although salvarsan does appear to act with astonishing promptness and efficacy in many cases, this is not true of all, and there have been numerous reports of unfavorable results. Paralysis of eye muscles, interstitial keratitis, gumma of the iris, papillitis and other ocular lesions have been cited after the use of salvarsan, these complications arising in general quite late after the use of the drug. Sufficient evidence has now been collected, however, to demonstrate that these accidents should not be attributed to the treatment by salvarsan, but result from a progression of the disease, as is evidenced by the fact that additional doses of the drug are usually followed by their disappearance.

SYPHILIS OF THE EAR.—Bradford A. Richards, Rochester, N. Y.  
New York State Journal of Medicine, 1918, vol. xviii, p. 58.

The weight of the late opinion is that salvarsan should be used in certain cases in combination with injections of a mercury salt, particularly where the manifestations of syphilis are active and the spirochetes are abundant. In latent lues more benefit seems to be derived from the old-fashioned mixed treatment; that is, mercury and iodides in a liquid medium, than from salvarsan or salvarsan and potassium iodide.

LUES OF THE NOSE AND THROAT.—Fred W. Bailey, Cedar Rapids.  
Journal of the Iowa State Medical Society, 1917, vol. vii, p. 446.

Symptoms of secondary syphilis in the nose are very similar to those of ordinary cold in the head. There is a burning sensation in the nose, and the patient is usually bothered a great deal with sneezing. Sore throat usually accompanies the nasal cases, and the patient often complains of headache, especially at night. The lesions of the secondary stage in the throat are the characteristic mucous patches, and cause considerable annoyance and pain in masticating and swallowing food. Mucous patches on the soft palate, pharynx, and tonsils cause severe pain referred to the region of the eustachian tube and ear when the patient swallows. The diagnosis is usually easy because the skin lesions usually precede the mucous patch stage. Enlargement of the cervical and other lymph glands together with the Wassermann test aid greatly in the diagnosis. Tertiary syphilis or gumma hardly ever appear sooner than two years after the initial infection. It may occur almost any time from two years on, as late as fifteen or twenty-five years or even more. In the nose and throat this stage is very commonly observed. The development is rapid and the destruction of tissue is very marked. The treatment of lues of the nose and the throat is, of course, generally, the same treatment as for syphilis of any other part of the body. Salvarsan



is the popular and most effective remedy, especially when supplanted by full courses of mercury and iodides. Syphilis of the nose and throat yield most readily to antisyphilitic treatment because of the abundant blood supply to these parts.

**GANGRENOUS SYPHILITIC GUMMA OF THE THIGH.**—A. Ravogli, Cincinnati. *Journal of Cutaneous Diseases*. 1916, vol. xxxiv, p. 353.

Between gummatous infiltration, disintegration, and gangrene, there is only a step. Gumma is the result of diseased lymph and blood vessels, which are narrowed or thrombosed; and in the same condition of the blood vessels in a more advanced stage is the cause of disintegration, necrosis, and gangrene of the elements forming the gumma. The rapidity of the spreading of the gangrenous process is mostly due to the quantity of the blood vessels involved, and to the presence of bacteria, together with a debilitated condition of the patient. In the tertiary or late period, when the patient is badly emaciated, the laboratory test may be in contradiction to the clinical symptoms from the inability of the system to produce antibodies, but this must be properly interpreted by the expert. In these conditions, a mild mixed treatment of mercury and iodides, associated with tonics, often gives much better results than the persistent administration of salvarsan.

**SOME POINTS RESPECTING THE LOCALIZATION OF SYPHILIS UPON THE AORTA.**—Oskar Klotz, Pittsburgh, Pa. *American Journal of the Medical Sciences*, vol. clv, p. 100.

Though we feel confident of the important part played by the lymphatic system of the thorax in localizing syphilis to distinct portions of the arterial wall, it is not clear as yet why and in what manner the virus finds its way to this particular region of the body. By analogy and in comparison with certain other infections, it is probable that the systematic distribution of the spirochete is accomplished by the blood stream. As with other infections, certain tissues and structures are more receptive for the metastatic infection than others. In some instances the localization of the infection may be associated with trauma, but this can hardly be a factor within the chest. Up to the present time animal experimentation has given no clue suggesting the reason for the thoracic metastasis in man. It is probable that the selection of the mediastinum by this infection is bound up with the question of the biological properties of the micro-organism and the favorable conditions presented by particular tissues for its growth.

**ACUTE YELLOW ATROPHY IN SYPHILIS.**—Stuart McDonald, Edinburgh. *British Medical Journal*, 1918, No. 2977, p. 76.

During the past two months the author has had the opportunity of studying in the postmortem room no fewer than five typical

cases of acute yellow atrophy, an experience which must be almost if not quite unique. Though numerous examples of subacute types of the disease have been recorded in recent years, and particularly in munition workers, typical cases of the classical icterus gravis are seen only at long intervals. In a personal experience of over 5,000 postmortem examinations performed since 1898 he has only investigated one other case. The present series of five cases have all occurred in syphilitic subjects in the course of, or subsequent to, treatment by "salvarsan" preparations and mercury; and considering the number of cases of syphilis now being treated throughout the country, a searching analysis of these fatal cases would appear to be urgently called for to determine, if possible, the relative parts played as etiologic factors by the syphilitic toxin, arsenic, and possibly some other exciting agent. In practically all the cases a full course of intravenous injections of salvarsan had been given, coupled with the usual intramuscular injections of mercury. Needless to say, in each case the diagnosis of syphilis was not only clear on clinical grounds, but was confirmed by a Wassermann test. These cases were not of undue severity, and indeed showed no special symptom of importance till a sudden onset of jaundice was noticed, without at first any special disturbance, the disease suggesting nothing more than an ordinary catarrhal jaundice. At a varying period of from two to eight days, however, acute symptoms appeared with dramatic suddenness. They were ushered in by a period of wild excitement and increased icterus, with hematemesis. The patients passed into a condition of deep coma, and death occurred in the five cases at periods of one to four days from the onset of the acute symptoms. The urine was markedly bile-stained, and in each case showed tyrosin; in some leucin was also demonstrated. In four of the cases diminution in the size of the liver was demonstrated during life. There is much to be said in favor of the view that in the causation of acute yellow atrophy we have two factors at least at work. It may be well that the typical condition is only produced when some special virus acts on a previously damaged liver. The most reasonable view to take would appear to be that the essential cause of acute yellow atrophy is some poison, possibly of microbial nature, produced in the alimentary tract and acting on a liver previously damaged, or whose function at least has been disturbed. The author has here five typical cases occurring together in a limited period; all have been syphilitic subjects and all have been treated with salvarsan preparations plus mercury. It is remarkable that though similar cases amounting to thousands have been treated by the same methods, such a complication as we have recently experienced has not been observed until now. This would seem to point to some other factor having been introduced. There is no evidence at present that the salvarsan has materially altered, at least in the last three years, and the syphilitic toxin and mercury factors may be taken as constant.

Together with this, we have the observation that in each case there was found at the postmortem examination microbial infection of a special type. There would appear at least to be a *prima facie* cause for regarding this infection as being the new factor which, acting on livers previously damaged by the syphilis, and possibly arsenic plus mercury, has completed the damage to the liver cells, and allowed autolysis of the tissue, which appears to be the essential liver change, to occur. Some such combination of circumstances might account for the rarity of the disease.

**SYPHILITIC ELEPHANTIASIS OF THE GENITALS.**—A. Ravogli, Cincinnati. *Lancet-Clinic*, June 17, 1916.

In all women the author has seen affected with extensive chronic genital ulcers of the phagedenic type, he considers these ulcers to be the result of a diffused gummatous infiltration and to produce destruction of the stroma of the skin. In some cases the infiltration may be absorbed, leaving a thick, heavy scar tissue as the result of proliferation of the connective tissues of the derma, but usually the skin breaks down, causing deep ulcers with hard infiltrated bases and hard thick edges covered with granulations. These ulcers tend to increase their surface by destruction of the skin and for a long time will not yield to local and general specific treatment. The ulcerative process, an open door for infectious elements, or the dead leucocytes, may be the cause of a chronic hypertrophic lymphangitis, which gradually produces a true elephantiasis of the vulva. In some cases, phlebitis of the saphena has been produced. This elephantiasis consists of a chronic hyperplasia of the connective tissues of the skin, and subcutaneous tissues; there is disproportion of the parts varying with the different degrees of the disease. Syphilis is, in these cases, the most common factor in the production of elephantiasis. The internal specific treatment with a base of mercury, or of arsenic, has had no results. The Wassermann tests in some cases have been slightly positive, in others negative. According to the general condition of the patient, the author has given mild specific treatment, small doses of calomel, or grey oil injections, and iodides of potassium and sodium, together with tonic preparations. Externally, no local application has been of any benefit. Of course, it is well to bathe with a mild solution of bichloride of mercury; or of bicarbonate of sodium to relieve the tension, and the irritation from the friction with pads of bichloride gauze. Surgical treatment must be employed.

**SYPHILIS OF THE LUNG.**—H. Lisser, San Francisco. *The American Journal of the Medical Sciences*, 1918, vol. clv, p. 379.

Syphilis of the lung is uncommon, but not extremely rare. It is worth diagnosing correctly. It does not produce a typical clinical

picture, easy of diagnosis. It should be kept in mind and ruled out in every case thought to be pulmonary tuberculosis where the sputum is negative for tubercle bacilli. Proper antisymphilitic treatment produces remarkable cures. Dr. Barker's advice is helpful (if you have a reliable serologist): "When in doubt, have a Wassermann test made; when not in doubt, still have a Wassermann test made."

A CASE OF TABES PLUS EPILEPSY WHICH THROWS LIGHT ON THE RELATIONSHIP BETWEEN LUES AND EPILEPSY.—G. S. Lundahl. Svenska Lakaresallskapetets Handlingar, 1917, vol. xliii, No. 3.

The author exhaustively describes the case of a laborer, aged forty-two years, with *sypphilis ignoree* who first developed typical cerebral lues, later tabes, and in association with the latter, epilepsy, without other etiology than lues. After a brief historical investigation into the older views of the relationship between lues and epilepsy, the author comes to the conclusion that all forms of epilepsy in syphilitics are dependent upon organic alterations in the brain. The epilepsy may be a local symptom of irritation resulting from syphilitic inflammatory processes in the motor centers or be of the genuine type and due to cicatrization following syphilitic or metasyphilitic alterations in the brain.

PRECOCIOUS SYPHILITIC HEMIPLEGIA.—P. Aveline and L. Babonneix. Journal de médecine et de chirurgie pratiques, 1917, vol. lxxxviii, p. 887.

The authors relate the case of a man aged thirty-six years who contracted syphilis in April, 1917, and sustained an attack of left-sided hemiparesis in August. In the meantime, he had been treated de rigueur with neosalvarsan, in all 7 injections with a total of 3.25 gm. of drug, and was discharged cured in July. The apoplectic attack had supervened very slowly and was several weeks in reaching its acme. The diagnosis rested on the lumbar puncture, which was rich in albumin and contained an abundance of lymphocytes. There were no other evidences of cerebral lues, such as pupillary disorders. Under a series of injections of cyanate of mercury, the patient improved so rapidly that at his own request he was discharged cured in three weeks. No true paralysis had been present at any time, either motor or sensory, the phenomena comprising muscular weakness and atypical sensory disturbances. The neosalvarsan injections had at first caused headache and vomiting, which disappeared during treatment. Since syphilitic hemiplegia is not supposed to appear before the sixth month, this case establishes a record.

PERSONALITY IN PARESIS.—Michael Osnato, New York. Journal of the American Medical Association, 1918, vol. lxx, p. 439.

In eleven out of twenty-five undoubted cases of general paresis reported in the original study, the influence of the individual's

make-up on the character of the reaction observed is conclusively shown. These were dispensary patients, about whom it was not always possible to obtain information as reliable and detailed as that obtained in the twelve cases reported by the author. Each one of the twelve cases is also undoubtedly one of general paresis, the diagnosis being confirmed by blood and spinal fluid examinations. In nine of these cases, the influence of the personality in determining the character of the psychotic reaction is conclusively shown. The other three also undoubtedly had general paresis, but the patients seem to have been normal before the inception of their disease, so far as their make-up could be determined. Grouping these thirty-seven cases, the author finds that in twenty of them it was possible to demonstrate his contention that paresis of the psychotic type occurs as a general rule in persons possessing abnormalities of make-up. In seventeen cases in which it was impossible to demonstrate this point, the paresis existed mainly as a physical disease, the physical signs of this condition being dominant. In neurotic persons infected with syphilis, the period of observation and treatment must be indefinitely prolonged because it is fairly evident that paresis occurs by preference in persons of this type.

EARLY SYMPTOMS IN LOCOMOTOR ATAXIA.—Edward Livingston Hunt, New York City. *The Medical Council*, 1918, vol. xxiii, p. 115.

There are five leading symptoms in particular with which locomotor ataxia inaugurates its attack on the nervous system. These are: (1) Pain. (2) Paraesthesiæ. (3) Bladder symptoms. (4) Blindness. (5) Gastric disturbances.

The most common and usual way in which the disease begins is with the appearance of pains. These pains are invariably described as sharp and shooting in character, short in duration, and in distribution particularly limited to the legs and thighs. They occur in paroxysms and last but a few seconds.

The second early symptom with which the disease begins is that known as paraesthesiæ. These paraesthesiæ are exceedingly common and occur in fully seven-eighths of the cases. Their distribution is very much like that of the pains; they almost invariably begin on the inner side of the thighs and extend down the leg to the feet. Later on in the disease, as the condition progresses, they involve the upper part of the body and include the arms and hands.

Disturbances in the action of the bladder are a very common manner for the disease to begin. In many spinal affections it is the first symptom and in locomotor ataxia is especially common. The mechanism of the bladder is poorly understood, and therefore it is difficult to explain the reasons for the various kinds of bladder disturbances which arise in spinal cord conditions. The most common ways in which bladder disturbances manifest themselves in

locomotor ataxia are twofold; either there is marked difficulty in emptying the bladder, or there is great difficulty in starting the stream.

Blindness is much less frequent as an initial symptom than either pain or bladder disturbances. It does not occur in more than 5 per cent of the cases. It very often does present itself in the very beginning of the disease. The pathology is that of a primary optic nerve atrophy.

Another method of onset in locomotor ataxia is by the development of symptoms referable to the stomach. This is present in about 10 per cent of the cases, being more frequent than eye symptoms, but not so common as bladder symptoms. The method of onset is threefold, pain, simple vomiting, or gastric crises.

ACQUIRED GENITAL SYPHILIS IN THE INFANT.—W. H. Haines, Philadelphia. *Journal of the American Medical Association*, 1918, lxx, p. 371.

A well-developed healthy boy, aged 16 months, of good disposition, was referred, March 7, 1917, for a single ulcer, the size of a dime, in the sulcus, just to the right of the middorsal line and extending back on the reflected layer of the foreskin. The foreskin was long, but retracted easily. The duration of the ulcer had been two weeks; it was noninflammatory; was not painful, and was typically indurated. It possessed the clinical characteristics of chancre in flopping over like a boat on retraction of the foreskin. It was positive for spirochete pallida. There was slight inguinal adenopathy. The patient received four injections of neosalvarsan, 0.15 gm., intramuscularly, at weekly intervals. The chancre was healed at the time of the second injection. At the time of the second visit, a profuse purulent meatal discharge was noted, which on appropriate staining was found to contain typical gonococci. The most probable source of infection was a colored nurse. A careful physical examination by the family physician revealed no clinical evidence of syphilis. She had very bad teeth; otherwise the examination was negative. Her blood gave a four-plus Wassermann reaction. Before noting the discharge from the meatus, we thought of transmission by some form of sexual perversion by mouth, but the family doubted this, as there was very little opportunity for her to practice it, and the presence of the discharge tends to preclude this idea. We can not help feeling that there must have been some evidence of syphilis around the nurse's genitals.

SYPHILIS AS A CAUSE OF STILLBIRTHS.—R. A. Bartholomew, Atlanta, Ga. *Journal of the American Medical Association*, 1918, vol. lxx, p. 291.

There is need for the adoption of a uniform definition of stillbirth and of compulsory reporting of stillbirths, in order that statistics

on this important cause of infant mortality may be improved. Syphilis is the causative factor in at least one-third of the stillbirths from the time of viability to full term, and a Wassermann reaction is strongly indicated in cases in which there have been suggestive clinical symptoms, unexplained abortions, or premature labors with macerated babies. A combination of mercury and salvarsan is more effective in assuring the birth of a healthy infant than salvarsan alone. Important confirmative evidence in the diagnosis of syphilis can be obtained from microscopic examination of the placenta, or in case of stillbirth, from examination of the fetal liver by the Levaditi method. More efficient and practical training in obstetrics, and safer surroundings for the patient during confinement will prevent some of the stillbirths resulting from other complications of pregnancy and obstetric emergencies. But there will always remain a considerable number of stillbirths from unavoidable causes.

INFANTILE SYPHILIS OF THE LIVER.—Edward L. Bauer. Philadelphia. *Archives of Pediatrics*, 1917, vol. xxxiv, p. 927.

The incidence of syphilis of the liver in infants is common enough, in fact, usually present in stillborn syphilitic babies. However, as an exclusive infection of the liver, with no other evidence of the disease, it is quite uncommon in the first year or two of life. The following case with the autopsy report is decidedly interesting from this viewpoint. F. D., a colored infant, was admitted to the Children's Hospital, Mary J. Drexel Home, when it was one year of age. The labor had been normal and the child in good condition, except for a "little cold" that soon cleared up. He weighed seven and three-quarter pounds at birth; was weaned at the expiration of two weeks, the change being made for the mother's convenience, and then fed on Mellin's food for one month. He vomited Mellin's food. Then several brands of condensed milk were tried until the tenth month. Up to this time, the child seemed to gain and develop normally, so he was given "table food." At the eleventh month, the abdomen began to swell, and the child became jaundiced. The urine was very yellow, discoloring the napkins so that the stain could not be washed out. The child developed a cough, becoming progressively worse, and a fever that seemed to become more intense daily. Physically, the child was markedly jaundiced, the skin dry and smooth, with no evidence of scratching or ulceration. Ears and nose negative; buccal mucosa pale yellow and the throat clean. It had three teeth. There were some rales in the lungs, and an impaired resonance. Heart sounds were feeble and embryocardiac. Abdomen was very distended and pendulous. The veins on the anterior wall, especially about the umbilicus, were very prominent and full. An umbilical hernia was present. There was a flaring of the lower ribs, and the liver could be felt, despite the distention. The edge seemed

rounded and smooth. Considerable fluid was present, and paracentesis only relieved the patient for less than a day. The spleen was not palpable. Extremities, bowing outward of both tibia; reflexes normal. There was no adenopathy. The temperature remained around 102° to 103° F. A Wassermann was positive plus 3. Father's Wassermann was negative. The mother gave a positive plus 2. The mother had been pregnant once before, giving birth to a full-term stillborn baby. The clinical picture presented by the patient was evidently the climax of an infection born in this child, and not giving symptoms until the eleventh month. Incidentally, it had been insured prior to the eleventh month, the examiner telling the parents that the baby was a "fine specimen." The autopsy showed that there was a diffuse hepatitis with intralobular sclerotic atrophy of the parenchyma, identified as lues; a passive congestion of the kidneys and a myocardial degeneration. No other lesions of any kind in any organ were found. The unusual feature was the localization of the disease to the liver. It was typical in that the occurrence of jaundice and ascites was late, but they are not constant in infants.

ANTENATAL SYPHILIS; SUGGESTED ACTION OF THE CHORIONIC FERMENTS.—Amand J. Routh, London. *Lancet*, London, 1918, vol. cxciv, p. 49.

The author's suggestions seem to point to the following conclusions, some of which are scientific facts, while others are nonproven, but he thinks, logical. The "granules" are the result of the "spirillolysis" or breaking-up of the spirochete pallida. The "granules" are infecting agents, being, in fact, spirochetes in the granule stage. They are able to develop into the mature spirochete in a suitable environment, or may become biologically inactive and remain latent for short or long periods. Chorionic (syncytial) ferments are present at the point of interdigitation of the fetal and maternal portions of the placenta. Their action is primarily trophoblastic to enable the delicate chorionic villi to penetrate the uterine mucosa and to open up maternal blood vessels, so that the ovum may find for itself a resting place with nutritive blood spaces around it. As a result of the destructive action of the ferments upon the maternal tissues so-called syncytiotoxins are formed, but appear to be at once neutralized by so-called syncytiolysins. If not thus neutralized, maternal and fetal toxemia may become present. The chorionic ferments (or their derivatives) are suggested as being capable of exercising their destructive properties upon the spirochete pallida, which may either be in the maternal intervillous or fetal intravillous tissues, both of which are in intimate relations with the syncytial cells of the villi whence the ferments arise. This destructive



action of the chorionic ferments upon the spirochete breaks it up into granules. The author further suggests that during pregnancy it is the continued action of the chorionic ferments upon the granules which may render them latent and biologically inactive, and perhaps in a few cases destroy them. After the pregnancy, when the chorionic ferments cease to be present in the tissues of the mother and child, the granules, wherever they may be, may develop into mature spirochetes. The success or failure of the chorionic ferments to protect the mother and child from spirochetal infection would depend upon (a) the virulence of the infection, which tends to diminish, owing to the presence of more maternal antibodies, with each successive pregnancy; and (b) upon the source of the infection. Infection is probably most difficult to arrest in a "mixed transmission" or in a true maternal infection, where attempts at infection of the embryo would be constantly proceeding throughout the pregnancy. It is probably least severe and most easily countered by the ferments when the primary infection is paternal, for it may then be a single infection only, and probably not capable of repetition if the primary infection be arrested. The Wassermann reaction of mother and child appears to be negative if infection has been by the spirochetes in their granule stage so long as the granules remain biologically inactive and the mature organism is absent.

ACUTE SYPHILITIC MENINGITIS IN AN INFANT TWELVE MONTHS OLD.  
—D. B. Leitch, New York. *American Journal of Diseases of Children*, 1918, vol. xv, p. 203.

The clinical picture presented by this infant closely resembled that of tuberculous meningitis. The gradual onset, the vomiting, the constipation, and drowsiness were all typical of that disease. Even in spite of three negative tuberculin skin tests and a diligent search for tubercle bacilli in the spinal fluid, it was thought probable that the case might still be tuberculous in origin. It was in the search for choroid tubercles that the first suggestion was obtained as to the true nature of the disease; and this led to an examination of the spinal fluid for spirochetes. From the presence of these in numbers the diagnosis was established. It was now apparent that the symptoms differed in some important respects from those of tuberculous meningitis: the continued absence of fever and convulsions, the turbidity of the spinal fluid and the relatively small percentage of lymphocytes. In other turbid spinal fluids, pyogenic organisms are regularly found. None were present in this case, either by smear or culture. Acute syphilitic meningitis in infants is a very rare condition and probably not more than half a dozen cases have been reported. In those cases which come to necropsy the spirochetes were demonstrated in the exudate at the base of the brain.

THE DIFFERENTIATION OF SYPHILITIC AND TUBERCULOUS PULMONARY LESIONS.—Walter C. Klotz, Los Angeles. *California State Journal of Medicine*, 1918, vol. xvi, p. 85.

The author finds that in thirty-one cases reported as pulmonary lues there were present symptoms and physical signs generally accepted as characteristic of pulmonary tuberculosis, and that in the majority of these cases a diagnosis of pulmonary tuberculosis had been made and that many of the patients had been treated as such. A subsequent diagnosis of pulmonary lues had been made only after the usual and accepted methods of diagnosis had been employed and additional facts obtained by careful histories and more thorough examinations. The experience and reputation of many of the authors reporting these cases would in itself assure us of the correctness of the diagnosis as reported. At the same time certain sources of error have been pointed out and conceded, while possible objections have been anticipated. At a time when many are beginning to recognize certain limitations and sources of error in the diagnosis of pulmonary tuberculosis, it may be well to recall other conditions that may bring about pulmonary changes. It certainly may be an error to make a diagnosis of tuberculosis on insufficient grounds and in so doing subject the patient to considerable loss, annoyance and worry. The clinical, social and economic significance of such errors is too obvious to require further discussion.

CERTAIN MARKS IN THE DIAGNOSIS OF ACQUIRED SYPHILIS.—R. M. LeComte, Washington, D. C. *Virginia Medical Semi-Monthly*, 1917, vol. xxii, p. 449.

The following are a brief set of rules that have been found of service in dealing with venereal sores and interpreting the results of the complement-fixation test for syphilis:

A. Every venereal sore should be examined with the aid of the dark-field microscope as early as possible, and this should be repeated several times in case spirochetes are not found at the first examination. Before telling such a patient that he is free from syphilis, he should be observed at intervals for a period of at least six weeks and a complement-fixation reaction done at the end of that time must be negative.

B. A positive Wassermann on the blood is conclusive only when:

1. There are distinct symptoms or signs attributable directly to syphilis, or
2. There is a definite history of previous infection or known exposure to infection (confrontation), or
3. The reaction is constantly positive in several tests taken at intervals, or is positive in high dilution.

C. A negative Wassermann on the blood is conclusive only when:

1. There are no signs or symptoms referable to syphilis discover-

able and no history of previous infection or possible exposure to infection obtainable, or

2. There is a definite history of syphilis, treated intensively and not succeeded by symptoms of the disease.

In the latter instance, one negative test does not mean that a cure has been effected. Before this can be said to have been obtained, the following should be secured:

D. 1. A negative blood test at frequent intervals and no symptoms for a period of two years during which no antisyphilitic treatment is taken.

2. A negative provocative Wassermann at the end of this time.

3. Negative spinal fluid findings at the end of this time, including normal cell count, globulin content, colloidal gold and complement-fixation tests.

HOW TO BE ASSURED OF THE NATURE OF A CHANCRE.—Tribondeau. *Archives de médecine et pharmacie navales*, 1917, vol. civ, p. 292.

Any clinical chancre may be followed by syphilis and in all cases there should be an immediate research for the spirochete before any treatment is instituted, (for treatment can cause the disappearance from the lesion of the latter). The same technic answers for the spirochete and Ducrey's bacillus. Smears should not be taken from surface pus but a juice should be extracted from the lesion itself. To this end the sore is thoroughly cleansed and a slight incision made with a bistoury in the zone of growth, the latter then being squeezed. The incised surface should then be curetted and smears made from the serosity. Two slides are mounted, one for a study of each micro-organism. The smear to be studied for spirochetes is treated with Ruge's liquid which contains formol; then with a mordant solution containing tannin and finally with the stain, Fontana's solution of ammoniated silver nitrate. The seroreaction is also practiced.

DIFFERENTIAL DIAGNOSIS BETWEEN SYPHILIS AND HERPES GESTATIONIS IN A RECENTLY DELIVERED WOMAN.—Sicilia, Madrid. *El Siglo Medico*, 1917, vol. lxiv, p. 896.

In the week before childbirth at term an ulceration appeared on the perineum which could have been confounded with total laceration. Two weeks later, an eruption appeared on the head, face, hands and soles of the feet. The character and grouping of the papules and pustules were very suggestive of syphilis. The eruption, nevertheless, could possibly have been herpes gestationis, and the author proceeds carefully to exclude the latter by clinical evidences. Serologic and bacteriologic tests are not mentioned.

EXPERIMENTAL SYPHILIS.—Uhlenbuth and Mulzer. *Berliner klinische Wochenschrift*, 1917, No. 27. Abstracted in the *Korrespondenz-Blatt für Schweizer Aerzte*, 1918, vol. xlviii, p. 31.

This work which was interrupted by the war, is still unfinished. It consisted of inoculating rabbits with the blood of early syphilis, with positive results in the testicles in a number of cases. Blood from subjects with active tertiary syphilis produced no positive results. It was also shown that in early syphilis the urine, saliva and sweat could not be made to transmit the disease to these animals. The blood in latent syphilis of any stage, with positive Wassermann, could not be made to give positive results. In other words, the positiveness of the seroreaction means nothing so far as inoculability is concerned. On the other hand, marked dilution of a spirochete culture (one spirochete to ten fields) does not abolish inoculability but is expressed by prolonged incubation period and low virulence. Incidentally it was shown that the spirochete is viable outside of the body, under favorable conditions for survival, at least forty-eight hours.

UNSUSPECTED SYPHILIS: A STATISTICAL STUDY.—James S. McLester, Birmingham, Alabama. *American Journal of Medical Sciences*, 1918, vol. clv, p. 320.

The object of this paper is to present certain statistical data drawn from the Wassermann reaction as applied to 567 consecutive private patients. Most of these patients were of the well-to-do classes, and all of them were seen in consultation, which fact warrants the assumption that they exhibited, as a whole, the more serious or puzzling diseases of inner medicine. None were supposed to suffer with venereal disease. Of these 567 consecutive patients, 94, or 16.5 per cent gave a positive Wassermann reaction; 7, with a negative Wassermann reaction, showed unmistakably clinical evidence of syphilis, thus bringing the known percentage of this disease to 17.8. These figures, then, represent a legitimate estimate of the frequency of syphilis in the better class of patients who suffer with the more obscure or serious medical syndrome. Among the 94 individuals whose Wassermann reactions were positive, only 27, or 29 per cent, admitted a venereal ulcer or other evidence of syphilis. It is startling to note that of this number 21 believed themselves cured, most of them basing their belief upon a physician's advice. Another group of 9, while categorically denying syphilis, gave histories which to the initiated pointed unmistakably to such an infection. Adding these 9 to those who admitted an infection, we have 36 patients, or 38 per cent, whose histories pointed with reasonable certainty to syphilis. The remaining 58 (62 per cent of the entire Wassermann positive group) gave no such history, direct or suggestive. It is interesting to inquire further into these 58 "Wassermann-positive,

history-negative" cases. Six on being confronted with a positive Wassermann reaction then recalled a long-forgotten venereal ulcer. The knowledge gained from a positive Wassermann reaction led always to renewed delving into family and past histories, and in 8 instances syphilis was thus found in husband, wife, or parent. Without the stimulating guidance of a known positive Wassermann reaction this information would have been lost. There were 10 others of this group who presented clinical evidence which, apart from the serum reaction, would alone point to syphilis. This included 4 instances of aortic aneurysm, 1 of aortitis, 5 of characteristic skin or throat lesions, 1 of a paroxysmal hemoglobinuria, 1 of characteristic neuroretinitis, and 1 of typical cerebrospinal fluid changes. Turning now to a consideration of the influence of syphilis upon the several internal organs, the heart and the aorta here, as always, are entitled to first place. It is difficult to differentiate invariably between essential myocardial disease, cardiorenal disease, and simple hypertension. In this series were 30 patients with essential myocardial disease, of whom 14, or 45 per cent, gave a positive Wassermann reaction. Four of the five patients with aortic aneurysm gave a positive Wassermann reaction. The arterial hypertension group presents a rather heterogeneous lot, for those are included who were with and without demonstrable arteriosclerosis, as well as those with and without kidney disease. There were 65 such patients, and 15, or 23 per cent, gave a positive Wassermann reaction. There were 26 patients who gave roentgenologic and other evidence of ulcer of the stomach or duodenum; 8 gave a positive Wassermann reaction, and 5 of these, under the influence of salvarsan as well as dietetic and other measures, have apparently recovered. Of 28 patients with pulmonary disease, apparently tubercular, 6 gave a positive Wassermann reaction, and of these 6 only 2 showed tubercle bacilli in their sputum; 5 were given antiluetic treatment, all of whom have experienced satisfactory improvement or cure, but since all had the benefit of the usual hygienic measures, conclusions are difficult. Observation of the roentgenologic signs and the clinical course in one of the patients at least, tempts the author to state unreservedly that he was dealing with syphilis alone.

WHAT IS THE SEROREACTION OF SYPHILIS?—Vernes, Paris Presse médicale, 1917, vol. xxv, p. 704.

The author's conclusions are, in part, as follows: Human serum in the presence of colloidal suspension of ferric hydrate will determine, or not, a precipitate, according to the periodic rhythm, which differs as the serum is, or is not, syphilitic. The curve will show that the suspension is less stable with the syphilitic serum. The result depends on the physical property of the suspension, and so far as the author has gone, the colloidal suspension of iron is the most

delicate. However, he hopes to discover one of still greater delicacy. The finer the flocculation of a stable suspension with a syphilitic serum, the greater the likelihood that it will not form flocculi with normal serum.

**SUBSTITUTION OF HUMAN BLOOD CELLS BY MONKEY'S RED CORPUSCLES IN PERFORMING THE COMPLEMENT-FIXATION TEST FOR SYPHILIS.**—Otto Schobl and Carlos Monserrat, Manila, P. I. *Philippine Journal of Science*, 1917, vol. xii, p. 253.

Human sera in quantities used for test were found to contain no antimonkey natural hemolytic amboceptor. Hemolytic sera of higher value can be obtained by immunization of rabbits with monkey's cells than it is possible by immunization with human red corpuscles. Comparative tests for diagnosis of syphilis carried out on samples collected at random gave identical results, whether anti-human or antimonkey hemolytic system was used.

**THE VALUE OF THE WASSERMANN REACTION AS INDICATED BY POST-MORTEM INVESTIGATION IN 331 CASES AT BELLEVUE HOSPITAL.**—Douglas Symmers and Charles G. Darlington with the collaboration of Helen Bittman, New York. *Journal of the American Medical Association*, 1918, vol. lxx, p. 282.

Depending on the antigen employed, the Wassermann reaction in the living patient, as carried out at Bellevue Hospital, gives a negative result in from 31 to 56 per cent of cases in which the characteristic anatomic signs of syphilis are demonstrable at necropsy. The Wassermann reaction in the living patient is positive in at least 30 per cent of cases in which it is not possible to demonstrate any of the anatomic lesions of syphilis at necropsy.

**THE USE OF LARGER QUANTITIES OF BLOOD SERUM IN THE WASSERMANN REACTION.**—E. H. Ruediger, Bismarck, N. D. *Journal of Infectious Diseases*, 1918, vol. xxii, p. 210.

Of fresh serum, quantities amounting to 0.2 of the total volume per test tube did not give false positive results and were but slightly anticomplementary. With larger quantities of serum a higher percentage of positive results is obtained. Glycerol is anticomplementary; the anticomplementary action may be overcome by increasing the quantity of amboceptor. Unconditional negative results should not be reported unless fairly large quantities of serum were used in the test.

**THE VALUE OF THE WASSERMANN REACTION IN THE NEWLY-BORN.**—H. H. Yerington, San Francisco. *Archives of Pediatrics*, 1918, vol. xxxv, p. 43.

A diagnosis of syphilis in an infant under 10 days of age can not be made by a positive cord or heel blood alone without evidence of

lues elsewhere. The results obtained from examinations of heel blood are more reliable than those obtained from cord blood, and a positive heel blood should be considered a danger signal. Whether a positive Wassermann in the mother, and also in both cord and heel bloods in the infant proves that the infant is luetic, is a question to be solved from later work. The placental work seems to show that although the blood of the mother may be negative, an active syphilitic process may go on in the placenta resulting in a stillbirth or abortion. How much reliance we can put on a suggestive placental report at this time is doubtful. This leaves us with the physical examinations of the parents and infants to go into, in which we are considering abortions, stillbirths, and other evidences of lues, the most important of all being the following-up of the infants, some of whom are now in their fifth year. If it is possible to have the children who are suggestive in this series examined carefully now for luetic manifestations and a Wassermann test repeated, with the addition of a luetin test, the value of the cord and heel bloods in their infancy can be fairly well determined. Only by carefully following up these cases for a period of years, retesting their blood from time to time, and giving them continuous treatment, can we hope to eradicate the later manifestations of the disease, which are so difficult to combat in later childhood.

**THE WASSERMANN REACTION.**—Frank E. Taylor, London, England. *Lancet*, London, 1918, vol. exciv, p. 20.

To estimate the strength of complement fixation of any serum giving a positive reaction, the test is repeated on that serum with five additional tubes, using the same reagents in the same quantities and in the same manner, but with a series of dilutions of the complement-fixing serum. Dilutions are made in watch glasses in a descending series of 1 in 4, 1 in 8, 1 in 16, 1 in 32, and 1 in 64; using 0.85 per cent saline solution as the diluent. After incubating and centrifuging, the amount of fixation is observed and noted. Thus if a serum shows complete fixation at a dilution of 1 in 8, partial fixation in dilutions of 1 in 16 and 1 in 32, and complete hemolysis in dilutions of 1 in 64, the results may be recorded thus: F/8. P/32, the dilution showing the end-points of complete and partial fixation being recorded, higher dilutions showing hemolysis. The value of the quantitative Wassermann reaction is shown to be particularly valuable in estimating the progress of a case while under anti-specific treatment.

**THE INTERPRETATION OF LABORATORY DATA IN SYPHILIS OF THE NERVOUS SYSTEM.**—Albert E. Sterne, Indianapolis, Indiana. *Mississippi Valley Medical Journal*, 1918, vol. xxv, p. 1.

A positive Wassermann, in the temperate zone, spells syphilis, and only syphilis. A negative or mild degree Wassermann does

not, by any means, indicate the absence of syphilis. Lues of the central nervous system is only a part of general constitutional syphilis, never occurs as a real entity and, furthermore, the nervous system is invaded early and not late, as is generally supposed. It is absolutely necessary, especially in doubtful cases, to correlate laboratory and clinical data. The Wassermann and other serologic tests are merely symptoms, which, like other physical signs, may or may not be present. They are extremely valuable, but not as determining as the objective clinical syndrome, notably when not definitely manifest. The laboratory is not a short-cut to diagnosis. Many laboratorians, while they may be excellent technicians, are incapable of determining the exact interpretation of the serologic reaction in debatable or doubtful cases. This decision rests with the clinician. Even with a positive Wassermann, a given symptom complex, in a knownluetie, is not always due to his syphilis.

**THE BRUCK PRECIPITATION TEST FOR SYPHILIS.**—Arthur William Stillians, M.D., Chicago. *Journal of the American Medical Association*, 1917, vol. lxix, p. 2016.

The Bruck precipitation test for syphilis fails in a considerable percentage of early secondary syphilis. It gives positive reactions in from 24 to 28 per cent of nonsyphilitics.

**DOES THE PARETIC GOLD-SOL CURVE IN PSYCHIATRIC CASES ALWAYS INDICATE SYPHILIS OF THE NERVOUS SYSTEM?**—Paul G. Weston, Warren, Pa. *American Journal of Insanity*, 1918, vol. lxxiv, p. 431.

In the course of fifteen hundred routine examinations of spinal fluid (Wassermann reaction, globulin tests, cell count and gold-sol reaction) it was found that the fluid from three patients, who had no history of syphilis and no positive Wassermann reactions and two negative luetin tests, caused a precipitate of colloidal gold in the paretic zone. These three cases were chosen because there was no history of syphilis,—and it is admitted that with the insane in particular, the absence of a history of infection is of little value,—and no laboratory evidence of syphilis other than the gold reaction. The author does not consider an increase of globulin or the presence of twenty or thirty cells, when taken alone, to be indicative of syphilis. He has repeatedly found an increase of the globulin in the fluids from patients who were not syphilitic. The question of whether the paretic curve ever occurs in psychiatric cases, not syphilitic, is left open.

**LUESERINE, AS A URINARY TEST IN SYPHILIS, ESTIMATE OF ITS VALUE.**—Y. Takeuchi, Japan. *Zeitschr. f. Derm. u. Urol.*, 1917, vol. xvii, p. 58.

The claim has been made previously that this test is positive in 100 per cent of syphilitics, and this led the author to investigate



its alleged value. His results in brief are as follows: In 32 cases of healthy and nonsyphilitic subjects the specimens of urine gave 16 positive and 16 negative tests. In 87 cases of syphilis, controlled by the Wassermann test, 54 specimens were negative and 33 positive. Of this total of 119 cases, 59 agreed with the Wassermann findings and the rest were at variance. Eight cases of syphilis in which the Wassermann was negative gave positive tests with lueserine. The details of the test are not given, nor is the method of preparation of the lueserine stated, but the inference is that the basis of the reaction is the presence of some special ferment in the urine of syphilitics not found in normal persons.

**REINFECTION IN SYPHILIS WITH OBSERVATIONS ON TWENTY-EIGHT CASES.**—Charles F. White, Major R.A.M.C., British Medical Journal, Oct. 20, 1917.

Careful investigation appears to establish that reinfection can take place, but that such reinfection can not take place until the original infection has been completely cured. The following conditions may be laid down: (1) In the first attack the spirochete being found from the chancre or syphilitic lesions, or the blood giving a positive Wassermann reaction, and (2) in the second attack, the spirochete being found from the new chancre which appeared at a different site from the first chancre, and the blood at the same time giving a negative Wassermann reaction, which, of course, implies that the patient must have been seen soon after the appearance of the second chancre, or at least before the blood had had time to become positive. If we can produce cases to fulfill these conditions we have very strong confirmatory evidence apart from our clinical observation and opinion that reinfection has actually taken place. The author cites twenty-eight cases apparently fulfilling these conditions.

**RELATIONS OF INFANT MORTALITY IN MOROCCO TO SYPHILIS.**—La Capere and Laurent, Fez. Presse médicale, 1918, vol. xxxvi, p. 13.

In Morocco there are no celibates and the polygamous wives are honored in proportion to the number of children they bear. Nevertheless, the country is not overpeopled, but underpeopled; a fact due entirely to the enormous infant mortality. To what extent is this due to syphilis? The authors selected 44 wives with Wassermann positive reactions, and learned that of a total of 248 children born to them but 74, or about 30 per cent, were still living. Certain families seem spared from infant mortality to the extent that a majority of the children are reared, but in most cases conditions were reversed and we find but 1 survivor in 6 and 7, 1 in 10, etc., or 2 in 6, 4 in 11, and so on. The authors took as controls 44 mothers with seronegative reactions who had borne 211 children and found

the proportion of survivors was 45 per cent, according to which syphilis slays 15 per cent of all children, an estimate certainly not too high. One should, of course, compare the deaths, not the survivors, 70 per cent in syphilitic women, 55 per cent in nonsyphilitic women.

VENEREAL DISEASES; THEIR RELATIONS TO INSANITY AND NERVOUS DISEASES.—John Joseph Kindred, Astoria, L. I. New York Medical Record, 1918, vol. xciii, p. 184.

Syphilis was the cause of 18 per cent of all the insanity in men and about 13 per cent in women, in 5700 first admissions, the total number of admissions of insane cases to the New York State Hospitals for the insane within a recent year. In other words, of 5700 insane men and women admitted during the year, 18 per cent were men suffering with paresis caused by or associated with syphilis, and about 13 per cent were women paretics or parasymphilitics, whose condition was due to or closely associated with syphilis. Notwithstanding this significant showing as to syphilis in its etiologic relations to insanity, only about 5 per cent of all syphilitics develop outright insanity. This would seem to prove that the cerebrospinal system in this 5 per cent is peculiarly susceptible to the syphilitic poison, particularly in those who have not been given to alcoholic and sexual excesses and undue mental worry and anxiety. In most cases of paresis, however, we have both susceptibility and a history of excesses. The fact that such a small percentage of syphilitics develop insanity, when we consider the mischievous effect of syphilis on so many of the bodily organs and tissues, leads us to the conclusion that syphilis after all, in many cases, may be considered to this extent a somewhat benign disease, especially if thoroughly and systematically treated from its incipiency by modern methods. While some of the roseate hopes for uniformly successful results of the salvarsan and neosalvarsan methods and other modern methods of treatment of tertiary syphilis, unfortunately, have been shattered, yet it can be conservatively claimed and proved that the modern treatment of tertiary, brain, and spinal syphilis has in many cases been positively brilliant.

THE PROPHYLAXIS OF VENEREAL DISEASE IN THE ARMY.—H. N. Cole, Cleveland, Ohio. Cleveland Medical Journal, 1917, vol. xvi, p. 601.

Venereal diseases are much more common in war times due to the laxity of morals and mode of life. As much as possible the Government must take stern measures. (1) To remove all alcoholic beverages from the neighborhood of soldiers. (2) Prohibit all street soliciting. (3) Have rigid supervision of all public houses in the army zones. (4) Prohibit the presence of all unessential females

from the war zones except when supplied with a military pass. (5) Because of the danger to others from these diseases all such fresh cases should be removed during the danger period to special hospitals in charge of specialists. (6) It should be a required part of every soldier's instruction that he receive an illustrated (lantern slide) syllabus or series of lectures drawn up by the proper officers showing the dangers of venereal diseases to him, to his family, and to the State, to show him the value of early diagnosis and treatment in such cases and the dangers of concealment, to show him that the best possible way to keep out of trouble is to avoid it, and to prove to him that professional prostitutes are just as dangerous as any others. Moreover, he should be taught that continence is not dangerous, but will make him of the most value to his country.

THE VENEREAL SITUATION AMONG THE FORCES AT WAR.—John C. Spencer, San Francisco. *California State Journal of Medicine*, 1918, vol. xvi, p. 10.

The military authorities of the world are agreed as to the devastating effects of venereal disease upon the enlisted men of the army and navy. Likewise they are agreed that fighting efficiency is the one requisite demanded of the troops. The overwhelming majority is agreed that prompt diagnosis and early and persistent treatment are the most vitally essential factors in reducing the amount of venereal disease and *eo ipso* keeping the greatest number of men efficient for fighting. All authorities are agreed on the fallaciousness of any system of segregation, regulation and inspection of prostitutes, under existing conditions, excepting those ruling in West Australia and Tasmania. Unless these obsolete and inefficient methods are capable of being carried out under a strict lock and key quarantine, their futility is absolute. Even under a fairly frequent system of inspection, there can be no escape from the great probability of an infection between inspections. The most fallible part of this archaic system is that of confining the inspection to one sex. The opinion is also practically unanimous, that until the whole civilized world is united on some method of prophylaxis more effective than the present moral and educational methods, in view of the proneness of the men in service, unless rigidly controlled by the military authorities, to indulge in impure sexual relations, some form of individual prophylaxis must be provided for them. Its use must be made compulsory, and the failure to use it penalized.

INVESTIGATION INTO THE ELIMINATION OF MERCURY.—J. Almquist. *Swenska Lakaresallskepets Hanolingar*, 1917, vol. xliii, No. 3.

The author arrives at the conclusion that in mercurial poisoning there is a vascular dilatation in several organs, in part of the arterioles and in a larger degree of the capillaries and venules, which is proba-

bly the result of a vascular paresis, due in turn to the action of the metal upon the nervous system. The vascular dilatation is most pronounced in the kidneys, gastroenteric tract, and liver; in other words, in the organs where the elimination of mercury is most active and where there is the greatest accumulation of the metal. The other structures to contain the latter were the pancreas, salivary glands, sweat glands and, in a slight degree, the sebaceous glands.

EXPERIMENTAL STUDIES OF THE MODE OF ABSORPTION OF MERCURY WHEN APPLIED BY INUNCTION.—Jay Frank Schamberg, John A. Kolmer, George W. Raiziss, and Joseph L. Gavron, Philadelphia. *Journal of the American Medical Association*, 1918, vol. lxx, p. 145.

Animal experiments demonstrate that the chief avenue of absorption of mercury, when applied by inunction, is the skin. Rabbits breathing a mercury-laden atmosphere may absorb considerable quantities of mercury through the lungs, but, as a result of the author's experiments, they believe the respiratory absorption to be far less important than the cutaneous absorption. Metallic mercury in the form of the official mercurial ointment is more volatile and is much more apt to be absorbed by the lungs, than calomel ointments of equal strength. Calomel ointments are fully as well absorbed through the skin as the ordinary blue ointment; indeed, the authors have the impression that calomel is absorbed with greater facility. There appears to be no reason why calomel inunctions should not supplant the unclean blue ointment rubbings which have been so long in use.

EXAMINATION OF URINE OF SYPHILITIC PATIENTS TREATED WITH VARIOUS PREPARATIONS OF JAPANESE-MADE SALVARSAN.—M. Maiye, Japan. *Zeitschr. f. Derm. u. Urol.*, 1917, vol. xvii, p. 67.

No difference was noted between the susceptibility to the action of the drug of males and females. As to age the albumin tests were: 17 cases, 17-30 years old, none positive; 10 cases, 31-40 years old, 2 weakly positive; 6 cases, 41-50 years old, 2 distinctly positive; 2 cases, 51-60 years old, 1 definitely positive. As to the stage of the disease: 1 case, primary, negative; 33 cases, secondary and latent, 2 weakly positive; 11 cases tertiary, 3 distinctly positive, 1 case hereditary, negative; 2 cases, tabes dorsalis, negative. The author feels that in view of the small number of patients whose kidneys are affected during treatment with these preparations and the short time it usually takes for the albumin to disappear spontaneously from the urine, there is no reason to decrease the dosage or prolong the interval.

## A PRELIMINARY REPORT ON THE USE OF AMERICAN-MADE SALVARSAN.—

H. Sheridan Baketel. Brooklyn, New York. The Medical Times, December, 1917, p. 337.

As soon as the governmental demands are satisfied, the medical profession will be supplied with a salvarsan equal in every respect to the product evolved by the late Prof. Ehrlich. Some thoughts come to mind in connection with the use of salvarsan, particularly as it has to do with reactions. Some practitioners commend or condemn salvarsan in direct ratio to the number of reactions which they observe. Reactions have numerous causes, very often only slightly connected with the drug itself. Wassermann blames the bacterial proteins in the water; Wechselmann, the rapid dissolution of great quantities of spirochetes and the freeing of their constituent parts. Some ascribe it to the "setting free of some toxic substances from the spirochete" and to the "liberation of endotoxins from the killed organisms" and to "imperfections in the physicians' technic" while still others, to impurities in the drug itself. Without doubt, each reason is tenable, and reactions might be caused even by two of the reasons ascribed. We are convinced, however, after a large experience in the administration of salvarsan that the febrile and gastrointestinal disturbances which may follow the injection will be found due to one or more of these causes: 1. Concentration of solution. 2. Presence of partially digested food in the gastrointestinal tract. 3. Imperfect cleansing of the alimentary canal. The use of a concentrated solution of salvarsan is inimical to the patient. Four decigrams of salvarsan should be dissolved in not less than 100 c.c. of sterile, freshly distilled water, and six decigrams in not less than 150 c.c. injected slowly. No food should enter the stomach for at least six hours before the injection or for four hours afterward. For that reason it is well to administer the drug late in the afternoon. The patient should have a complete catharsis the morning of his treatment, so that the intestinal canal may be free from extraneous material. If the precautions are insisted upon by the physician, he will have little cause to worry over the liberation of endotoxins, the pranks of bacterial proteins in the water or the impurity of the drug. The first two causes are largely theoretical, and the elaborate laboratory tests on animals to determine the toxicity of the drug place the latter cause largely in the realm of imagination. Proper technic, freshly distilled water and enough of it, and a clean, empty tract from stomach to anus will reduce reactions to an infinitesimal minimum.

LUARGOL IN HUMAN THERAPEUTICS.—R. Dalmier. *Annales De L'Institut Pasteur*, 1917, vol xxxi, p. 516.

The action of luargol upon the spirochetes, also upon the lesions caused by these parasites, is more elective, more specific than that of arsenobenzol. From the standpoint of the fixation reaction one

obtains in the primary and secondary cases of syphilis equivalent results with 1 gr. 50 to 2 grams of luargol and with 2 to 3 grams of arsenobenzol; so that in using the two products in equal doses, which is quite possible, one can obtain a greater proportion of cures with the first. The comparative study of the percentage of arsenic in these different products proves that the increase in the parasiticide power of luargol comes from the addition of silver and antimony. Luargol lends itself to the realization of a very active antireactional chemical vaccination. The chemical immunization of the organism, ordinarily useless, has the advantage of defending the exceptional intolerances which are able to manifest themselves and extend the bounds of classical contraindications of chemotherapy.

OBSERVATIONS ON THE INTENSIVE COMBINED TREATMENT OF SYPHILIS.  
—J. H. Stokes, Rochester, Minnesota. *Mississippi Valley Medical Journal*, 1918, vol. xxv, p. 12.

In the author's employment of salvarsan, both alone and in combination, he thinks constantly in terms of the following principles: The drug as such and its impurities seems to be more toxic or at least its toxic effects seem more serious in the vascular mechanism than in any other group of structures. Its effect on the kidney in moderate dosage is negligible. He has given it several times in cases of advanced chronic nephritis, with a phenolsulphonephthalein functional test of 0 to 2.5 per cent, without injury and even with actual improvement in the condition of patients with syphilis. Acute renal reactions (anuria) are, he believes, primarily glomerular (vascular) injuries, most of which have occurred following too high an initial dose, acid salvarsan, and in pregnancy. The immediate effects of salvarsan on the disease are those of the complex amino-arsenic molecule, or of a "salvarsanoprotein." The late complications following its administration are those of arsenic, which is especially stored in the liver, spleen, and skin. Late complications due to cumulative effects and arsenical injuries must be constantly watched for. In the first injection or two, salvarsan causes a therapeutic shock, the Herxheimer reaction, which is dangerous in proportion to the importance of the structure most involved by the infection. This has special reference to the meninges and brain, the myocardium, and other vital structures. Even a Herxheimer reaction in a gummatous larynx may asphyxiate the patient unless preparation is made to meet it. Salvarsan is primarily a spirocheticide. It suppresses contagion and clears up lesions, but its effects are transient, and must always be followed up by mercury. Mercury, on the other hand, is an inferior spirocheticide. It will not control contagious lesions but it is a better builder of immunity. Little salvarsan is worse than none at all, especially in early syphilis, and its indiscriminating or overcautious use leads to premature tertiarsm. Old salvarsan should be preferred in early and latent syphilis,

wherever there is hope of radical results. The author prefers neosalvarsan in visceral syphilis and in children. He utilizes the experimentally demonstrated affinity of neosalvarsan for the meninges in the treatment of late syphilis of the nervous system, and avoids it when the process in the nervous system is acute, or likely to be unfavorably influenced by meningeal irritation.

IMAMICAL, ONE OF THE NEWER REMEDIES, 2ND REPORT ON ITS USE IN SYPHILIS, INFECTIOUS JAUNDICE AND RAT-BITE DISEASE.—T. Ito, H. Matsusaki, Japan. *Zeitschr. f. Derm. u. Urol.*, 1917, vol. xvii, p. 16.

Further trial has convinced the authors of the remedy that it is as valuable as claimed in the earlier reports, and they are more confident as to the conditions determining its use. For an ordinary, well-nourished, syphilitic patient the subcutaneous dose is 1.0 c.c. daily for 3 days, then on alternate days till the twentieth dose in 0.5 c.c. doses. A special refined quality is used for intravenous injection in doses of 3.0-5.0 c.c. at intervals of 5 days, with a certain amount of freedom for the exercise of judgment as to interval and dose. In case the latter method is used, it is followed by a course of intragluteal injections of 10-20 doses. One patient received as high as 61 doses, but others did not need so much. A few doses only were required to remove, or greatly modify, the symptoms of frank cases of early syphilis, whereas longer treatment is needed in the tertiary cases. Reactions have not been especially annoying, but did occur in some cases of subcutaneous use after the fifth to sixth dose or after the first intravenous dose. The reaction consisted of fever and headache, symptoms of intoxication which the authors attribute to the toxic action of the bacteria as these are destroyed in the system. Stomatitis was rarely encountered, but a mouth wash is advised. There was no pain following the injections, and any tendency to induration at the site of inoculation could be removed by gentle rubbing for a few minutes. In animals a diarrhea was one of the signs of overdosage, but in the amounts advised for syphilis this is not likely to occur. On the contrary, there was constipation, as a rule, so that a mild laxative may be needed. Care should be exercised to avoid leakage of the solution into the tissues at the site of injection, and as the drug is insoluble in alcohol and ether, the tincture of iodine should be used with great caution.

SIX HUNDRED AND SIX OR THE GERMAN POISON.—Gaucher, Paris. *Annales des maladies veneriennes*, 1917, vol. xii, p. 705.

Under this sensational title Professor Gaucher seeks to prove that salvarsan never cures, and is always a menace. This attitude goes back to 1911, and months before the war he had published his facts. He accuses the drug of aggravating the disease and of actually pro-

ducing the so-called metasymphilitic diseases. Its favorable action is but momentary. Recently under a prolonged course of salvarsan injections patients have actually developed general paralysis. The drug can bring it on in an old tertiary case or at an early period. Before the introduction of 606 did anyone ever hear of general paralysis developing within a year, and tabes at the end of three years? The drug can skin over an ulcer and thereby fool us as to its true character. It may hold back the disease in its evolution, but only at the expense of aggravating it.

HEMATOPORPHYRINURIA DUE TO SALVARSAN.—Cavina, Bologna. *Giorn. ital. d. mal. veneree e della pelle*, 1917, vol. lviii, p. 315.

The author examined the urine in 50 subjects who had received intravenous injections of salvarsan in regard to the presence or absence of a hematoporphyrin content. This substance is also known as hematin without iron, Preyer's hematin, etc., and contains neither iron nor albumin. It has been found in the urine in numerous affections and also after injection of certain drugs. It was learned that in about 40 per cent of patients who received intravenous injections of salvarsan in therapeutic doses there was a greater or less degree of hematoporphyrinuria. It was assumed that the injections are responsible for increased or abnormal destruction of a certain quantity of hemoglobin with resulting production of porphyrin. The mechanism may involve a temporary insufficiency of the liver which ordinarily disposes of destroyed hemoglobin.

THE TOXICITY OF NEODIARSENOL.—Erwin P. Zeisler, Chicago. *Journal of the American Medical Association*, 1917, vol. lxix, p. 2181.

In a recent series of twenty intravenous injections given to fifteen dispensary and private patients in all stages of syphilis, the author has noticed an unusually large percentage of reactions. Ten of the patients complained of varying degrees of nausea, vomiting, headache, and fever for from twenty-four to forty-eight hours after the injection. One woman with a fresh syphilitic infection (roseola, adenopathy and a positive Wassermann reaction) five days after the administration of 0.6 gm. of neodarsenol developed fever, headache, vertigo and incessant vomiting which lasted twelve hours. In the absence of any other explanation, the author was forced to conclude that this was a late toxic manifestation, possibly an encephalitis. The patient recovered under rest in bed. Another patient in the midst of the injection complained of nausea, faintness, and thoracic oppression, with marked flushing of the face. He was immediately given a hypodermic of epinephrin and was able to go home half an hour later. Another patient with symptoms of early tabes collapsed after the injection, became extremely pallid, and his pulse became almost imperceptible. The immediate reaction in this case



was most alarming, but fortunately he recovered. A very obese patient on account of technical difficulties received 0.6 gm. of neodiar-senol intramuscularly. The pain and local reaction were so intense as to require morphin injections for the next forty-eight hours.

**SULPHUR WATERS IN SYPHILIS.**—Durand-Fardel. *Presse médicale*, 1918, vol. xxxvi, p. 32.

This resource is very ancient, not only as an antisyphilitic *per se*, but because of its reputed diagnostic power in bringing to light a latent syphilis, in the absence of which one could prognosticate a radical cure. But any direct specific action has never been shown, and even if the sulphur can provoke an outbreak of latent infection, the Wassermann has rendered such a procedure unnecessary. In the old days of hydrargyrisms, the sulphur spring may have rendered great service in aiding the elimination of mercury; and today when intensive mercury cures are in vogue, it may still have its uses. In fact it is a matter of proof that the elimination of retained mercury may be hastened. Sulphur spring water can also offset some of the effects of syphilis, notably anemia, and it is also of value in hastening the disappearance of obstinate skin lesions as well as tertiary deposits anywhere in the body. In addition to drinking the water, full baths, vaporizations, inhalations and even hypodermoclysis may be used, as throughout the past. Thus far we know nothing of the interreactions of sulphur and arsenobenzol.

**TREATMENT OF LEUCOPLASIA BUCCALIS.**—Avezou. *These de Paris*, 1917, Abstract in *Journal de médecine et de chirurgie pratiques*, 1917, vol. lxxxviii, p. 728.

The author obtained remarkable results in obstinate cases with interstitial injections of sterile water. The addition of cocaine and adrenaline makes the treatment more endurable, but does not add to its value. The injections are indicated in well localized and circumscribed patches. A very fine needle is used and the amount of solution injected should not exceed half a cubic centimeter. This is thrown in slowly, but little time is required. As a result the patch assumes a peculiar appearance, likened to the texture of orange peel. For about 24 hours the tongue is somewhat sore. For several days the patch is only reddened but at the end of a week it is thickened and elevated, with a macerated appearance. The opaline or porcelain look has vanished. At the end of a fortnight the patch has entirely sloughed, leaving a smooth red surface, which soon forms new papillæ and epidermis. In certain cases there may be a recurrence, requiring a second treatment.

**TREATMENT OF SYPHILIS.**—Dujardin, Havre. *Archives Médicales Belges*, 1917, vol. lxx, p. 1116.

The author, after an elaborate account of various plans of treatment of 731 cases of syphilis in soldiers, asks himself how many were

really cured. Of very recent cases he thinks "many" were cured, because they went for ten months or more without evidences of recurrence, treatment having been suspended. As far as the others are concerned, he would not care to suspend the treatment even if the seroreaction became negative. These subjects had undergone two or three intensive cures. In order to make a rule, he would give each case of this sort four periods of treatment, without regard to negative seroreaction. Even then he would not regard these men as cured if clinical relapses or meningeal reaction had occurred within the first year of the disease. He deprecates the point of view that the "chances" are in favor of a patient's being cured.

EMETINE AS AN ANTISYPHILITIC AND ANTIYAWS SPECIFIC.—Da Matta, Manaus. Bulletin de la Societe de Pathologie Exotique, 1917, vol. x, p. 863.

The author at the beginning of a short contribution on the treatment of yaws (Castellani's treponemosis) with arsenicals and emetine, recalls that some years ago Millian obtained remarkable results from emetine in lingual syphilis which could not be reached by mercury or salvarsan. He cured a case of ulcer at the base of the tongue in this manner. The author was therefore led to test emetine in yaws. By combining it with salvarsan he obtained a brilliant cure, the patient presenting, before treatment, over one thousand lesions. The term "boubas" for generalized yaws appears to have been used in Brazil for over 200 years, although in Spain it originally meant syphilis. The emetine was given by intravenous injection, from five to ten cgms. of a 1 per cent solution, every other day.

WAR SYPHILIS.—De Napoli. - Giornale Italiano della Malattie Veneree e della pelle, 1917, vol. lviii, 225.

As a rule syphilis with open lesions requires isolation. Soldiers with chaneroids need not be interned *per se*. The nonulcerated primary sclerosis of course requires isolation of the patient for obvious reasons, but chiefly because of the opportunity gained for intensive treatment and the resulting protection of the patient, his family, present or future, and the public. Early intensive treatment does not always cure, but delays and attenuates the general explosion. When the lesions do appear they will be contagious, and not alone when seated in the mucosae. Were it not for this source of danger, ambulatory treatment would answer. Arsenobenzol is indicated in the earliest stages, but after the disappearance of secondary lesions intramuscular injections of insoluble mercurials lend themselves best to ambulatory treatment. For troops on the march, solutions of mercurials for buccal administration are preferred by the author to pills. The office of the arsenicals is to sterilize, to heal

the contagious lesions, in a word to transform open syphilis into closed syphilis; but when this stage is reached the treatment changes from arsenic to mercury. As for tertiary lesions they are bound to be rare, owing to the youth and physical condition of the troops.

TREATMENT OF SYPHILIS IN THE ARMY.—Harold N. Cole, Cleveland, Ohio. *Cleveland Medical Journal*, 1917, vol. xvi, p. 601.

From the standpoint of the individual, of the army, of the public and of the state's welfare, our freshly syphilized soldiers should be treated in special base hospitals for these cases. These hospitals should be under the direction of competent specialists in dermatology and syphilis, and have the laboratory facilities so essential for the early diagnosing and proper treatment of syphilis. Each hospital should have a dentist associated. The treatment should be of the most vigorous type and designed to clear up the patient's condition as soon as possible, to return him to the trenches as soon as possible, and yet to keep him out of the hospital as long as possible. This can only be done by a series of six to eight salvarsan (or one of its congeners) injections, five days to one week apart, accompanied by as much mercurial treatment as the patient can stand. This patient must later have some ambulatory mercurial treatment from time to time. If these measures are not carried out, innocent cases of syphilis will be very common among our soldiers, in the end there will be more sick days in the army, the army strength will not be at its maximum, and in the future the soldier, his family and the state will have to suffer the consequence.

INFLUENCE OF SALVARSAN ON THE COURSE OF PARALYSIS AND TABES.—Sommerfelt. *Norsk Magasin for Laegevidenskaben*, 1918, vol. lxxix, p. 115.

This article is an abstract of one by Treupel, which appeared in the *Berliner klinische Wochenschrift*, 1917, No. 39. In 1909 Alt claimed good results from salvarsan in paralysis. Spiethoff obtained only negative results in paralysis but saw improvement in six cases of tabes. Treupel has treated five cases of paralysis, two of taboparalysis and three of tabes. His conclusions are as follows: in the early stages of paralysis the disease shows some response to treatment but a period is sooner or later reached in which the results become negative. The same judgment holds good for taboparalysis. In pure tabes, on the other hand, there may be essential improvement under salvarsan and this improvement is maintained.

TREATMENT OF SYPHILIS OF THE EYE.—A. Poulard. *Presse médicale*, 1917, vol. xxxv, p. 648.

When the disease attacks the eye, as in iritis and choroiditis, no time is to be lost. Daily for three days, 1 cgm. of cyanate of mer-

cury should be given intramuscularly, followed by the same dose on alternate days. Apparently nothing is gained by using the intravenous route. If, after a week the disease has not been arrested, neosalvarsan should be given, preferably by intravenous injection, although the author does not hold the general opinion that this drug should never be used by the other routes. He instills it into the conjunctival sac in affections of the cornea and iris, and has practiced the subconjunctival injection in severe iritis. Mercury is the remedy of first choice, and the cyanate the salt of first choice. (It exerts the same activity in specific meningitis). The intramuscular method is the route of first choice, and, as a rule, the inunction cure, mercurials by the mouth and iodides play only a minor role. The author does not shrink from the intramuscular use of neosalvarsan, because of its great convenience and because he finds no drawbacks to such use.

THE TREATMENT OF SYPHILIS OF THE BRAIN AND CORD BY SUBDURAL INJECTIONS OF SALVARSANIZED-MERCURIALIZED SERUM.—S. T. Nicholson, Clifton Springs, N. Y. *New York State Journal of Medicine*, 1918, vol. xviii, p. 70.

The methods of choice of intraspinal therapy: (1) The salvarsanized serum of Swift and Ellis. (2) The Ogilvie method. (3) The Byrnes method which has been the basis of the author's report. One and three the author has used combined and his results have been so encouraging that he will continue the method described. However, as it has been shown that salvarsan is not found in the blood an hour after injection he bleeds the patients earlier and in addition has what Byrnes claimed at the time of his original publication, the beneficial effects of a mercurialized serum due to the patient's having previously been treated by general mercurial therapy. Every worker in this field should, however, be equipped to follow any form of the treatment. Finally, the method of choice in the author's hands is the mercurialized-salvarsanized serum intraspinally primarily because the treatment is elastic and may be easily adjusted to the individual problem presented by each case. For example, if a patient has any intravenous salvarsan reaction, the intraspinal treatment may be delayed several days or one has the option of using a mercurialized instead of a salvarsanized-mercurialized serum.

REMARKS ON INTRACRANIAL TREATMENT OF SYPHILIS OF THE OPTIC PATHWAYS AND OPTIC ATROPHIES.—Mark J. Schoenberg, New York. *New York State Journal of Medicine*, 1918, vol. xviii, p. 62.

Begin the treatment as early as possible. That means make a diagnosis of the very beginning of *lues nervosa*. Syphilographers

of great experience, like J. A. Fordyce, and neurologists, like Nonne, put great stress upon the treatment of lues nervosa at its earliest appearance. Treat energetically. The most improvement is obtained during the first course of treatment. The subsequent treatment prevents recurrences and aims at a "cure." Know when to discontinue the treatment and watch the patient after its cessation. When the patient is and remains free from clinical as well as from serologic manifestations, treatment should be discontinued. Do not delay the intraspinal or intracranial treatment, as soon as indicated. Do not forget the patient and his vitality or general condition. Respect and stimulate the natural defensive properties of his tissues by prescribing the old time-honored, general hygienic rules. Eradicate all the foci of infection (bad teeth, old gonorrhea, nasal sinusitis, chronic tonsils, etc.) Individualize the treatment because no two individuals are alike as regards their response to treatment. Do not forget the general practitioner. Teach him to think neurologically when he has to treat a patient with syphilis. We know that there is a meningeal reaction concomitant with the cutaneous eruption and the cerebrospinal lues has many a time, if not always, its inception during the secondary stage of syphilis. Let the physician know when this takes place and begin immediate, appropriate treatment. This may obviate an involvement of the parenchyma of the nervous tissue in the future and may prevent the optic atrophies. No diagnosis of syphilis is complete unless the spinal fluid is examined.

INTRAVENTRICULAR INJECTION OF ANTISYPHILITICS IN PRIMARY OPTIC ATROPHY, REPORT OF A CASE.—Michael Goldenburg, Chicago. *Annals of Ophthalmology*, July, 1917.

The lethal issue of this case, in the author's opinion, justifies no definite conclusion as to the merits of direct intraventricular antiluetic medication. Certainly, the observations made after the first and subsequent injections do not tend to prove that this method of treatment is valueless, or without promise of hope for this disease. It must be taken into consideration that the patient came under our observation at a time when the luetic infection had made such deep inroads on the central nervous system that all physical findings left no doubt as to the diagnosis of general paresis. The hopelessness of his general condition is certified by the utter failure of the customary constitutional treatment. When finally it was decided to endeavor to reach the optic nerves through the skull, his condition had reached a stage where a cure must be looked upon as almost miraculous. As ophthalmologists we are not primarily interested in the general neuropathologic condition, and it is encouraging to note that in spite of the heroic measures instituted, not only was no harm produced, as is evidenced by several reports from the attending physician of the institution of the insane to which the

patient was confined, but that, if anything, the usual progressive process of optic atrophy was for a time at least arrested, so that limited vision was present practically to the very instant of death, where otherwise total blindness in all probability would have been the result without this method of treatment.

**PERMEABILITY OF THE MENINGES TO ARSENIC IN PARESIS AND TABES.—**

J. Henry Barbat, San Francisco. *Journal of the American Medical Association*, 1918, vol. lxx, p. 147.

The technic which the author employed is as follows: The patients were given intravenous injections of either salvarsan, neosalvarsan or arsenobenzol. Within twenty minutes the spine was tapped, and the fluid was allowed to run until it barely dropped, the quantity varying from 30 to 60 c.c. The fluid was collected in two portions. The first was tested for colloidal gold, Wassermann, Pandy, Nonne and Noguchi reactions, and the second portion for arsenic. In ten cases, 20 c.c. of blood were withdrawn within half an hour after the administration of the arsenic. This was allowed to clot, the serum was removed, and both clot and serum were tested for arsenic. Twenty-four hours after the spine was tapped, a second tapping was done, removing at least 10 c.c., though usually twice that amount was removed. This fluid was also examined for arsenic. Analyses showed that the blood serum contained more than five times as much arsenic as the clot contained, and that it averaged only about eight parts per million. This fact proved that within half an hour after the administration of 0.4 gm. of salvarsan, 75 per cent is fixed in the body cells. The second portion of spinal fluid, which was withdrawn immediately after the administration of the salvarsan, showed 31 per cent arsenic-free and 27 per cent with a trace, while 42 per cent gave an average of 0.2 part per million. The spinal fluid withdrawn twenty-four hours later showed one case out of twenty-six arsenic-free, two cases with a trace, and an average of 0.25 part per million in the remaining twenty-three cases. These figures would indicate that arsenic can be made to pass into the spinal fluid in more than 96 per cent of patients suffering from tabes or paresis, by the technic which the author describes.

**PROPHYLAXIS IN CEREBROSPINAL SYPHILIS B. C. Corbus, Chicago.**

The *Journal of the American Medical Association*, 1917, vol. lxxix, p. 2089.

In cerebrospinal syphilis the ideal method of prophylaxis consists in attacking the disease during the primary stage. If correct diagnosis is made and energetic treatment instituted at this period there should be no further signs of the infection, and subarachnoid involvement would be unheard of. The general aim in treatment, especially among otologists, laryngologists and ophthalmologists, seems

to be the healing of the superficial lesions only. Lumbar puncture, with negative spinal fluid findings, is demanded in every case as final evidence of cure, no matter how energetically the treatment has been carried out. As a check on possible future complications involving the nervous system, lumbar puncture, with spinal fluid examinations, is demanded in every patient who presents himself for treatment after the primary period. In view of results of the author's experience, extending over a year, with intensive salvarsan treatment and mercury rubbings, with spinal drainage, it is his belief that these constitute the most effective mode of treatment, at the same time causing the least danger to the patient.

**INTRASPINAL TREATMENT OF SYPHILIS OF THE CENTRAL NERVOUS SYSTEM.**—Homer F. Swift, New York. *Journal of the American Medical Association*, 1917, vol. lxix, p. 2092.

In considering the treatment of syphilis of the central nervous system, it is not advisable to throw all the various forms of the disease into one class and have a hard and fixed method of procedure for all. It is always well to separate, so far as possible, the symptoms that are the result of active disease from those that are the result of scars. Obviously, one does not expect to restore scarred nerve tracts or centers. The elimination of active syphilitic foci and the arrest of a progressive degeneration are the objects of our therapeutic efforts. In the large majority of the tabetics in whom the Wassermann reaction was rendered negative in the blood and spinal fluid, there has been no progressive downward course as determined in periodic clinical examination. On the other hand, in those tabetics in whom it was impossible to influence appreciably the abnormal laboratory findings, the disease was often progressive. The cerebrospinal fluid from these resistant cases often showed a gold curve of the parietic type, and probably the persistence of the Wassermann reaction was due to the parietic nature of the disease. It is the author's experience, in common with most other workers, that our therapeutic efforts in paresis lead to little more than an increase in the number and length of the remissions. The disease usually terminates fatally. The period of useful life, however, seems to be lengthened, and the period of hospital confinement shortened. In considering intraspinal treatment, it is well to differentiate sharply between the injection of salvarsan or neosalvarsan in amounts or concentrations that are injurious to the spinal cord, and the injection of serum, perhaps reinforced with a fraction of a milligram of salvarsan, which is practically never followed by any bladder or rectal disturbance. Although such serum contains only minute quantities of salvarsan, the fact that it is definitely spirocheticidal has been established by several workers.

## BOOK NOTICES

(Books for review should be sent to Dr. W. H. Deaderick, Associate Editor,  
Dugan-Stuart Bldg., Hot Springs, Arkansas.)

NEUROSYPHILIS, MODERN SYSTEMATIC DIAGNOSIS AND TREATMENT.—Presented in One Hundred and Thirty-seven Case Histories. By E. E. Southard, M.D., Sc.D., Bullard Professor of Neuropathology, Harvard Medical School; Director Psychopathic Department, Boston State Hospital; etc., and H. C. Solomon, M.D., Instructor in Neuropathology and Psychiatry, Harvard Medical School; Acting Chief-of-Staff, Psychopathic Department, Boston State Hospital, etc.; With an Introduction by James Jackson Putnam, M.D., Octavo, 500 pages, with 25 full page illustrations, \$5.00. Boston, W. M. Leonard, Publisher. 1917.

This book is written primarily for the general practitioner, and secondarily for the syphilographer, the neurologist and the psychiatrist, and is based on the analysis of one hundred and thirty-seven case histories from the Psychopathic Hospital, Boston, the Danvers State Hospital, and cases from private practice. The work is divided into seven sections: I. The nature and forms of syphilis of the nervous system. II. The systematic diagnosis of the forms of neurosyphilis. III. Puzzles and errors in the diagnosis of neurosyphilis. IV. Neurosyphilis, medicolegal and social. V. The treatment of neurosyphilis. VI. Neurosyphilis and the war. VII. Summary and key. In two appendices are described the technic of the laboratory tests and of the common methods of treatment. The authors are confident that no one can now successfully make a differential diagnosis between the parietic and the diffuse nonparietic forms of neurosyphilis in many phases of either disease, even with all laboratory refinements, and conclude that it is improper not to give the full benefits of modern treatment to all cases in which the diagnosis remains doubtful. Graphic charts are included, classifying anatomic and clinical forms of neurosyphilis, and excellent illustrations add greatly to the value of the book. The authors are warm advocates of very intensive treatment in syphilis of the nervous system, and a spirit of optimism colors their prognosis in many of these cases. The summary and key add to the reference value of the work. Under laboratory methods, the authors state that the Wassermann and the Bruck tests agreed positively in seventy-four cases, negatively in twelve instances, and were at



variance in fifteen. The authors claim that the advantages of the test are the short time required to do the test, the limited amount of apparatus necessary, and the simplicity of the technic. The disadvantages seem, for the most part, to be bound up in the personal variations that are apt to occur. Their method of intensive treatment consists of intravenous injections of salvarsan or its substitutes, repeated twice a week over a period of a number of months, together with injections of mercury salicylate once a week, potassium iodide by mouth, and intraspinal injections as indicated. The monograph is one of the most valuable contributions on neurosyphilis which has appeared in years.

**SIFILIS PULMONAR.** By Dr. C. Patino Mayer. 420 pages, with 25 engravings and 9 colored plates. Buenos Aires, E. Spinelli, Publisher. 1916.

This exhaustive work embraces five chapters, covering the history of syphilis of the lung, pathology, frequency and localization, classification, symptomatology, diagnosis, complications, treatment, and experimental syphilis. The author divides syphilis of the lung into three types, the tumorous or gummatous, the pneumonic, and the form characterized by cavity. The cuts are good and the colored plates of the very highest class of workmanship. The bibliography, covering twenty-eight pages, adds to the research value of the work. Those familiar with Spanish will doubtless find this monograph of supreme interest.

## VALUABLE SUGGESTIONS FOR CONTRIBUTORS TO THE AMERICAN JOURNAL OF SYPHILIS

"The four rules for the preparation of an article will then be: (1) Have something to say; (2) Say it; (3) Stop as soon as you have said it; (4) Give the paper a proper title."<sup>1</sup>

Let your phraseology express one meaning and one only. Be clear.<sup>2</sup>

**Manuscript.**—Manuscripts should be typewritten, with wide margins, and double spaced, on one side of paper 8½ by 11 inches in size. The original copy should be sent to the "Journal" and the carbon copy retained by the author. Number the leaves consecutively, beginning with the title page. Put your name and address on the manuscript.

**Illustrations.**—Illustrations should be clear, preferably pen-and-ink drawings. Of photographs send a good print rather than a negative. Have lettering parallel to the bottom and top margins, and of sufficient size to be clear if cut is to be reduced. Tracings should be in black-and-white; avoid colors. Write your name on back of each picture; number them in one series (Fig. 1, etc.) to the end, and indicate in margin of the manuscript about where each is to be printed. See that the text references and "figures" correspond. Legends for illustrations should be written on a separate sheet.<sup>3</sup>

**Bibliographic References.**—Give only references actually consulted. If an article is known only through an abstract give reference to the abstract in addition to that of the source. References are printed to be of help in further reading; therefore they must be complete, concise, and correct. Follow the style of the "Index Medicus" and "Index-Catalog of the Library of the Surgeon-General's Office." Be conservative in the use of abbreviations.<sup>4</sup>

**Arrangement.**—As authors are quoted in the text give each a number in the order of citation, and number the bibliographic reference with the same number. Arrange the references in a list at the end of the article in the order of the numbers (see below), or arrange items in alphabetical order according to last names of authors, and distinguish between articles by the same author by the use of the date after his name in the text.

**Foot-notes.**—Where an author wishes to use foot-notes at bottom of each page instead of the bibliography at end of article, the foot-notes should be written in the text, but separated from it by horizontal lines above and below, or *better*, place them at bottom of each page. Use figures to indicate these foot-notes, and number consecutively (1, 2, 3, etc.) throughout the article. If in addition to the bibliography mentioned above it is desired to use foot-notes on certain pages, these can be indicated by an asterisk (\*).

**Final Reading.**—Let some one other than the author read the manuscript with these directions in mind.

**Shipment.**—Send manuscript flat, postage paid, to the associate-editor, Dr. Wm. H. Deaderick, Dugan-Stuart Building, Hot Springs, Arkansas.

**Proof-reading.**—Read carefully, with special attention to spelling of names and bibliographic data. Make corrections *in the margin* only with lines drawn from the revision to the point of change in the text. Answer queries in the proof by making correction or crossing out the query. Verify your references from the sources, not from your carbon copy.

### References. (Read these.)

<sup>1</sup>Billings, J. S.: Our Medical Literature, Trans. VII Intern. Med. Congress, Lond., 1881, i, 54-70.

<sup>2</sup>Mayer, Emil: Medical Literature and its Preparation, Med. Record, N. Y., 1915, lxxxvii, 1019-1021.

<sup>3</sup>Allbutt, T. C.: Notes on the Composition of Scientific Papers. London, Macmillan, 1904.

<sup>4</sup>McCrae, Thomas: The Use of Words, Jour. A. M. A., Chic., 1915, lxxv, 135-139.

<sup>5</sup>Suggestions to Medical Authors, issued by the A. M. A. Press, Chic., A. M. A., [1914 (?)].

<sup>6</sup>Place, F.: Bibliographic Style in Medical Literature, Med. Record, N. Y., 1913, lxxxiii, 157-160.

# The American Journal of Syphilis

A QUARTERLY JOURNAL DEVOTED TO THE  
STUDY AND PREVENTION OF SYPHILIS

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## Original Articles

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### THE NEW PATHOLOGY OF SYPHILIS\*

BY ALDRED SCOTT WARTHIN, PH.D., M.D., ANN ARBOR, MICH.

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(Received for publication, July 1, 1918)

IN an analysis of 4,880 autopsies performed at Bellevue Hospital during a period of ten years Symmers† found anatomic evidence of syphilis in only 314 cases, or 6.5 per cent. In a similar study made by myself of 750 autopsies at Ann Arbor during the last ten-year period evidence of syphilitic infection was found in 300 cases or in 40 per cent of the entire autopsy material. Nothing could better illustrate and emphasize the points which I hope to establish in this paper than the wide discrepancy between these two studies. This is made all the more striking when the character of the clinical material in the two hospitals is considered. In a great city hospital like Bellevue, in a great city like New York, with patients derived chiefly from the poorer classes, the incidence of syphilis

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\*Delivered before the Harvey Society, at the Academy of Medicine, New York, December 8, 1917.

†Journal of the American Medical Association, 1916, lxvi, 1457.

would naturally be thought to be much greater than in a state hospital, like the university hospitals at Ann Arbor, in which the clinical material is drawn chiefly from the rural population of the state, representing the better elements of the middle class farmers, village storekeepers, mechanics and laborers. Is the latter rural population syphilized to a greater extent than the poorer working classes of New York? In 139 autopsies made at Ann Arbor in 1916-1917, fifty-six cases showed evidences of active syphilis, in 1915-1916 out of 79 autopsies there were 30 cases, and in 1914-1915 out of 58 autopsies there were 25 cases, and for the remaining years the incidence was 40 to 50 per cent annually. Does this mean a greater total incidence of syphilis in Michigan than in New York?

I believe that this striking difference in findings is chiefly dependent, not upon the clinical material, but upon the *different pathologic criteria employed in these two studies*. If we turn to Symmers' paper we find that the criteria employed by him were chiefly anatomic. His diagnoses were based upon the following lesions: Aortitis in 55.7 per cent of cases, aneurysm in 25.6, chronic interstitial orchitis in 39, lesions of the nervous system in 35.6, of the liver in 33.4, of the skin in 33.4, indurative atrophy of the base of the tongue in 25, osseous lesions in 14.9, of the respiratory tract in 10.5, of the lymph nodes in 6, and of the gastrointestinal tract in 2.2 per cent. It is very evident from Symmers' paper that many of the findings not classed as gummata were in reality gummatous processes and should have been classed as such. For example, *hepar lobatum* always means healed gummata of the liver. He takes no note of syphilis of the heart muscle, the pancreas or adrenals, or of the occurrence in the most varied tissues of small inflammatory infiltrations associated with the presence of the *Spirochete pallida*. In short his diagnoses have nothing to do with the spirochete and the most common lesions produced by this organism; but are based chiefly upon the gross pathologic anatomy of pre-spirochete days.

The pathologic anatomy of syphilis is still ruled by the dicta of the gross pathologic anatomists of the latter half of the last century. The statements in our textbooks concerning the pathology of this infection in its latter stages *are based almost without exception upon the occurrence of the gumma, and syphilis of an organ is said to be frequent or rare according to the frequency of gumma of*

*that organ.* The gumma was practically the only anatomic lesion of syphilis recognizable by the early pathologic anatomists. Morgagni's knowledge of the gross pathology of syphilis (*lues venerea*) consisted almost wholly of observations upon gummatous lesions of the bones, aneurysm of the aorta, and changes in the lungs and kidney. He speaks particularly of never finding changes in the liver in bodies affected with the *lues venerea*. As it was not until the years 1831-1837 that syphilis was separated from gonorrhea and soft chanere by Ricord, there was no advance made in the pathology of syphilis in the first thirty years of the nineteenth century.

It is a very strange fact that Rokitansky, the father of modern gross pathologic anatomy, in the thirty thousand autopsies said to have been performed by him, should have added nothing to the knowledge of the pathology of syphilis. With a pathologic material drawn from a highly infected population his observations upon the gross pathologic anatomy of syphilis are amazingly few. Ulcers near the nails, necrosis and hyperostoses in bones, and inflammations of fibrous structures, and possibly gummata, constitute his apparent knowledge of this disease, as shown by his great work on gross pathologic anatomy. Virchow, likewise, in his *Cellular Pathology*, 1858-1860, barely mentions syphilis and, at that, not in connection with any essential pathologic feature of the disease. Nevertheless in 1858\* he clearly distinguished the simple inflammatory (irritative) and the gummatous lesions of syphilis, and showed for the first time the part played by this disease in producing inflammatory conditions of the most varied organs and tissues. This article really laid the foundation for the modern knowledge of the pathology of syphilis obtained since the spirochete was discovered. But his separation of syphilitic lesions into the two types made little impression upon the syphilology of the next forty years. In Wagner's *Textbook of Pathology* (1862-1876), emphasis of the *syphiloma* (tuberculum s. gumma syphiliticum, tumor gummosus, gummy tumor) as the essential pathologic lesion of syphilis ruled completely the minds of both clinicians and pathologists up to nearly the close of the century, and still remains the chief part of the pathology of syphilis in our textbooks. This nar-

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\*Ueber die Natur der constitutionell-syphilitischen Affectionen, Arch. f. Path. Anat. u. Phys., xv, 217.

rowing of the conception of the pathology of this disease was largely due to the very valuable and comprehensive article by Baümler on syphilis in the von Ziemssen's Handbook (1874). The chapter on the general pathologic anatomy of syphilis in this article concerns itself chiefly with Wagner's conception of the syphiloma; Baümler's monograph has been the fount of inspiration for the majority of textbook articles on syphilis written since 1875.

As the relationship of tabes and paresis to syphilis became more evident during the next two decades the conception of "postsyphilitic," "metasyphilitic," and "parasyphilitic" processes arose in explanation of this relationship. Fournier (*Les affections parasymphilitiques*, Paris, 1894) was chiefly responsible for the use of this term and for the view that a large number of pathologic conditions bore a definite relationship to syphilis, but were not syphilis and were not necessarily caused by it. Paresis, tabes, aortic aneurysm, arteriosclerosis, a variety of conditions of the nervous system, leucoderma, leucoplakia, and many other affections were regarded as parasyphilitic affections. The association of a typical form of aortitis with aneurysm, paresis, tabes, and other parasyphilitic conditions gradually led to an acceptance of its syphilitic origin and nature. Nevertheless, up to the discovery in 1903 of the *Spirochete pallida*, the gumma remained the one specific histopathologic lesion of syphilis.

With the discovery of the etiologic agent of syphilis it was to be expected that a change would be wrought in our concepts of the pathology of the disease, and that expectation was soon fulfilled. Parasyphilis has disappeared as the various parasyphilitic affections have been shown to be active syphilis with living spirochetes still present in the affected tissues. The term is now a misnomer. To the pathologic criteria of the disease there have been definitely added during the last decade the characteristic lesions of the central nervous system and syphilitic mesaortitis. The Harvey lecture by Fordyce in 1915 on "Some Problems in the Pathology of Syphilis" expresses very fully the generally accepted knowledge of the pathology of syphilis of the present day. He recognizes that "in all stages and in all organs the lesion begins in the perivascular lymph spaces as a lymphocytic and plasma-cell infiltration;" but he still says that "the type of lesion of the tertiary period is the gumma."

He advances the pathology of syphilis only by the full recognition of the syphilitic nature of the nervous lesions and mesaortitis. Of the pathology of latent syphilis in other organs and tissues he has this to say: "Aside from gummatous involvement of the viscera, little is known of the effects of the infection on the various organs." My investigations and their results begin here in the demonstration that the gumma is not the type of lesion of late or latent syphilis, and that the viscera are involved in all cases of latent syphilis, not by gummatous processes, but by specific inflammatory processes, eventually fibrosis, usually mild in character, but acquiring pathologic importance because of their progressive character.

As soon as the Levaditi method of demonstrating the *Spirochete pallida* in sections was published, I began investigations as to its occurrence and distribution in the tissues, and my attention was first drawn to congenital syphilis because of the greater ease of demonstrating the spirochetes in the tissues of such cases. As a result of such studies important facts concerning the incidence of *Spirochete pallida* in the heart muscle of congenital syphilitics have been added to our knowledge, as, for example, the constant presence of spirochetes in the hearts of cases of congenital syphilis dying before or at birth, the occurrence of focal fatty changes in the myocardium due to the colonization of the organism, and of a specific type of interstitial myocarditis due to the same cause. The essential lesion in congenital syphilitic myocarditis was shown to be edema of the interstitial tissues, often giving reactions for mucin, infiltration with lymphocytes and plasma cells, and fibroblastic and angioblastic proliferations. Spirochetes were found to be constantly present in such lesions, often in enormous numbers. That spirochetes could be present in great numbers in the tissues of congenital syphilis without producing tissue changes was also shown.

From the study of the lesions of congenital syphilis it was a natural step to that of the pathology of acquired syphilis. Similar lymphocyte and plasma-cell infiltrations associated with spirochete localization were found in the tissues and organs of known cases of acquired syphilis, aortic aneurysm, tabes, paresis, etc., but it was not possible to demonstrate the presence of spirochetes so readily or in such a large proportion of cases, owing to their smaller numbers and widely scattered distribution. Nevertheless, the demon-

stration of the organism was successful in such a large number of cases (75), as to make the specific syphilitic nature of these lesions certain. In the progress of these studies the specific inflammatory lesions of spirochete localization have been found in the myo-, endo-, and pericardium, the aorta, pulmonary and other large arteries, nervous system, liver, pancreas, adrenals, testis, prostate, prevertebral and mesenteric tissues. These lesions vary greatly in size, from minute collections of few cells to larger infiltrations just visible to the naked eye. Every stage of development, from the early active lesions to complete healing and fibrosis was observed; but no cases were found in which there were no active lesions. Complete healing throughout the body was never observed. The marked tendency of the lesions to undergo fibrosis and healing with the formation of dense hyaline scar tissue was a striking feature and regarded as evidence of the relatively avirulent character of the organisms. Spirochetes may be found in all stages up to nearly complete healing, but were never found in the dense fibroid areas. A detailed description of these lesions of latent syphilis will now be given.

#### THE MICROSCOPIC PATHOLOGY OF LATENT SYPHILIS

*Nervous System.*—The central nervous system was examined in only a small percentage of the material, the head much more frequently being opened at autopsy than the spinal column. No especial study was made of either brain or cord, and the changes noted in these were only those found in the ordinary routine of microscopic examination accorded all tissues and organs obtained at autopsy. The most constant changes were those found in the *meninges*. In practically every case of latent or clinical syphilis autopsied some degree of thickening of the meninges was noted. The dura was constantly more adherent and thickened. No active syphilitic foci were however, ever found in this membrane. Focal thickenings of the leptomeninges were found in practically every case. These varied in all possible degrees. They were most common over the parietal convolutions, and along the median surfaces, being most easily seen over the sulci. They more frequently involved the arachnoid than the pia; but the focal thickenings very frequently represented fibroid areas involving both pia and arachnoid. Thick-



ening of the wall and more or less obliteration of the meningeal vessels were usually found associated with the localized fibrosis. In the great majority of the brains examined these meningeal focal thickenings were small, usually pinhead in size, and sharply circumscribed. Only in clinical cases of paresis, tabes, cerebral syphilis, cerebral gumma and "toxic psychosis" were they larger, more diffuse and more marked. Transition stages from these small focal lesions to the larger ones were found. The great majority of these focal fibroses of the leptomeninges were healed inactive areas, plasma-cell infiltrations and fibroblastic infiltrations being found only in the more active cases of syphilis. They appear in the latent cases to represent old and early lesions in the history of the individual infection. The occurrence of active lymphocyte and plasma-cell infiltrations in the meninges in old latent cases of syphilis seemed, however, to parallel the degree of activity of the lesions found in the heart, aorta and other tissues. Precisely the same lesions in the meninges occurred in the nonparetic and nontabetic cases of syphilis as in those showing a clinical paresis or tabes, the only difference being one of degree. Active meningeal lesions have been found more frequently in young adults with congenital syphilis than in the old cases. Similar lesions occur in the meninges of the cord; and, as in the case of the cerebral meninges, the degree of these meningeal changes usually corresponded to the severity of the lesions in other organs and tissues. The meninges of the cord usually showed the most marked changes in cases of tabes and paresis, but a few exceptions to this were found in latent cases. The meningeal changes noted by me associated with syphilis, both latent and clinical, correspond in general with those described by LeCount and other writers as characteristic of meningeal syphilis. The focal chronic leptomeningitis regarded by some writers as the result of chronic alcoholism, would appear from my experience to be the result of syphilitic infection rather than of alcoholism. It is true, that some of my most marked cases of meningeal fibrosis were both alcoholic and syphilitic; but precisely the same meningeal changes occur in those cases without a history of alcoholism.

Focal infiltrations of lymphocytes and plasma cells were found in both *brain* and *cord* in cases not regarded clinically as paresis or tabes. These infiltrations were perivascular and were sometimes

associated with proliferative changes in the vessel, at other times not. The character of these minute scattered lesions is precisely identical with those found in the brain and cord, in paresis and tabes, the differences being only those of number and degree. In two cases diagnosed clinically as "toxic psychosis" these lesions in the brain were so numerous as to suggest a pathologic diagnosis of early paresis. Two other cases without nervous symptoms gave similar microscopic findings. In one case of secondary syphilis dying from salvarsan poisoning the brain showed scattered perivascular plasma-cell infiltrations.

The question is raised by these findings as to their frequency in syphilis and their relation to the symptoms of paresis and tabes. Is every case of syphilis, to a slight degree, at least, a parietic or tabetic? There can be no doubt that pathologically there are borderland cases just as there are clinically such; and my experience would lead me to believe that probably every case of old syphilis will present in the brain and cord the same scattered perivascular infiltrations of lymphocytes and plasma cells found in all other organs and tissues. Such infiltrations represent simply the local reaction to the presence of spirochetes; and their relation to paresis and tabes may be simply one of degree, with reference to the number of infecting organisms, the degree of intoxication produced, and the resulting destruction of nerve tissue and functional disturbance produced.

Minute infiltrations of lymphocytes and plasma cells are of frequent occurrence in and about the *spinal ganglia*, the *spinal nerves* and the large *peripheral nerves*. No spirochete studies have been made of these, and their syphilitic etiology is assumed because of their identity with known syphilitic lesions in other organs and tissues, and their constant association with such.

Similar infiltrations are also very common in and about the *sympathetic nerves* and *ganglia*, particularly in the solar plexus and periadrenal plexus. Fibrosis, atrophy, and pigmentation of these ganglia have been observed in connection with such infiltrations. In three cases of Addison's disease due to syphilitic fibrosis and atrophy of the adrenals, the adrenal and solar plexus showed especially marked syphilitic infiltrations.

The tendency of the nervous system to spirochete localization

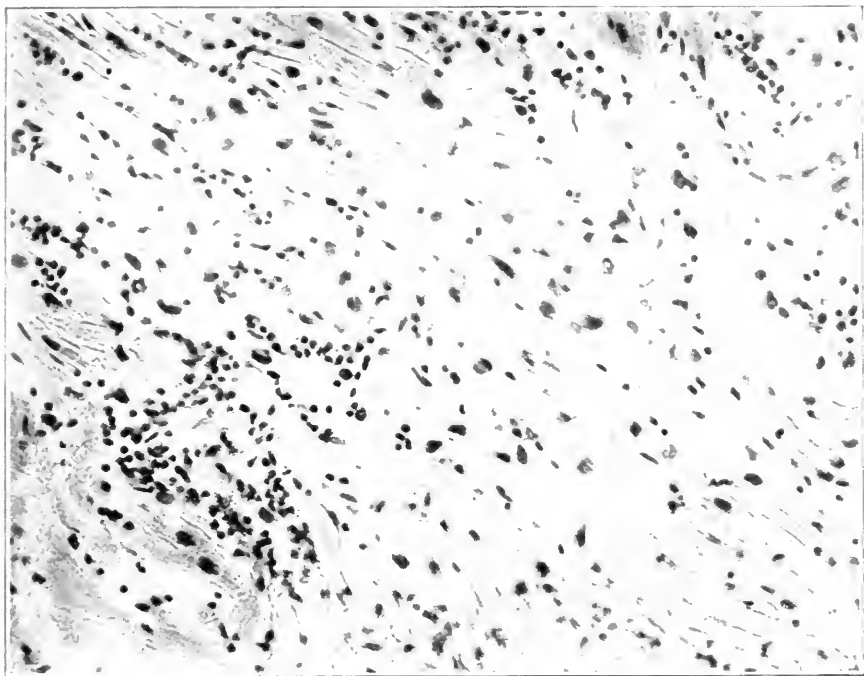


Fig. 1.—Chronic syphilitic myocarditis. Unsuspected latent syphilis. Sudden death. Male, aged 52 years. Dilatation of left ventricle. Wall of ventricle showed diffuse plasma-cell infiltrations. Spirochetes present throughout these infiltrations.

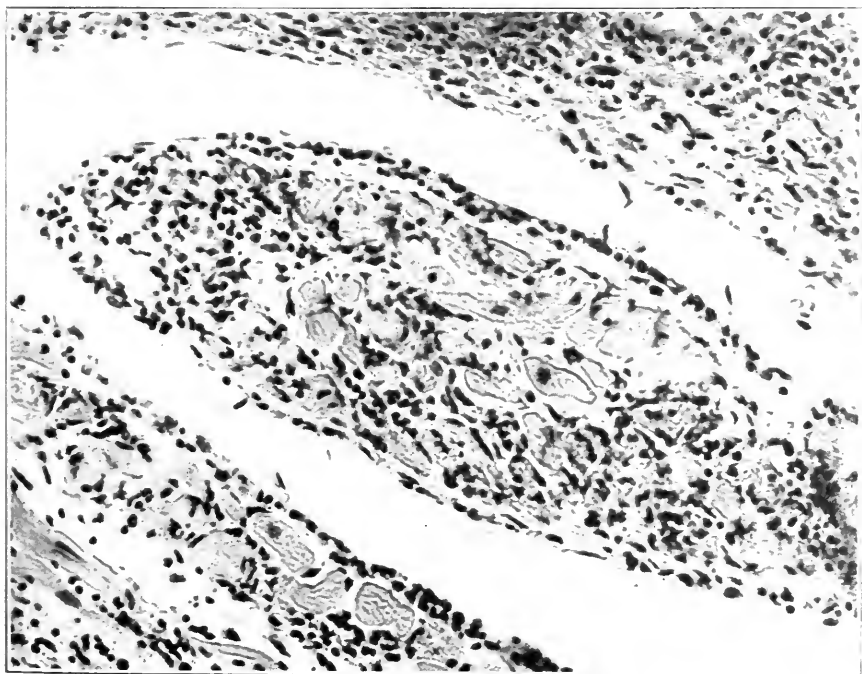


Fig. 2.—Chronic syphilitic myocarditis. Male, 45 years of age; sudden death. Syphilis not suspected by clinicians; aneurysmal dilatation of left ventricle at apex. Diffuse plasma-cell infiltration of papillary muscles and wall of left ventricle at apex. Spirochetes present.



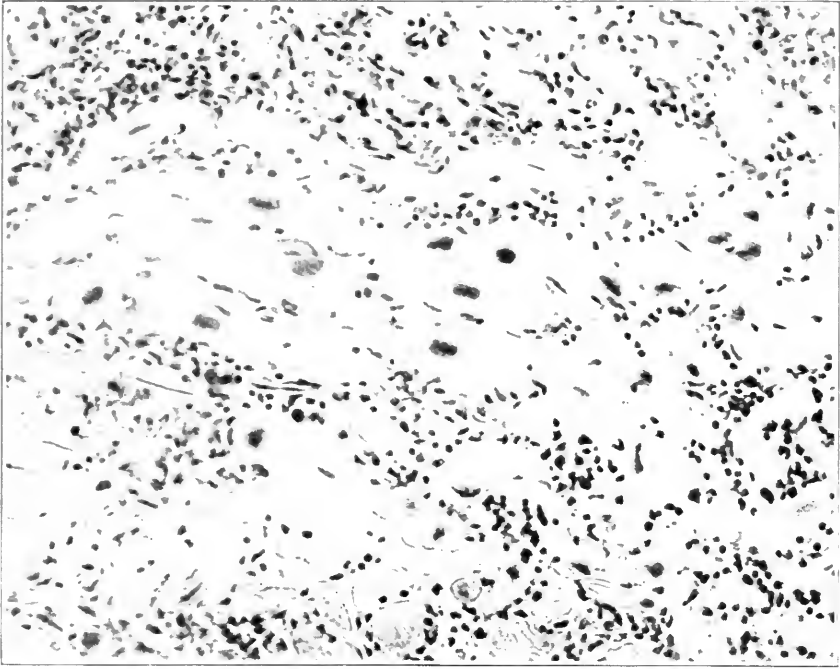


Fig. 3.—Chronic syphilitic myocarditis. Unsuspected latent syphilis in middle-aged man, sudden death. More severe process than in preceding. More marked plasma-cell infiltrations of left ventricle wall above apex. Spirochetes.

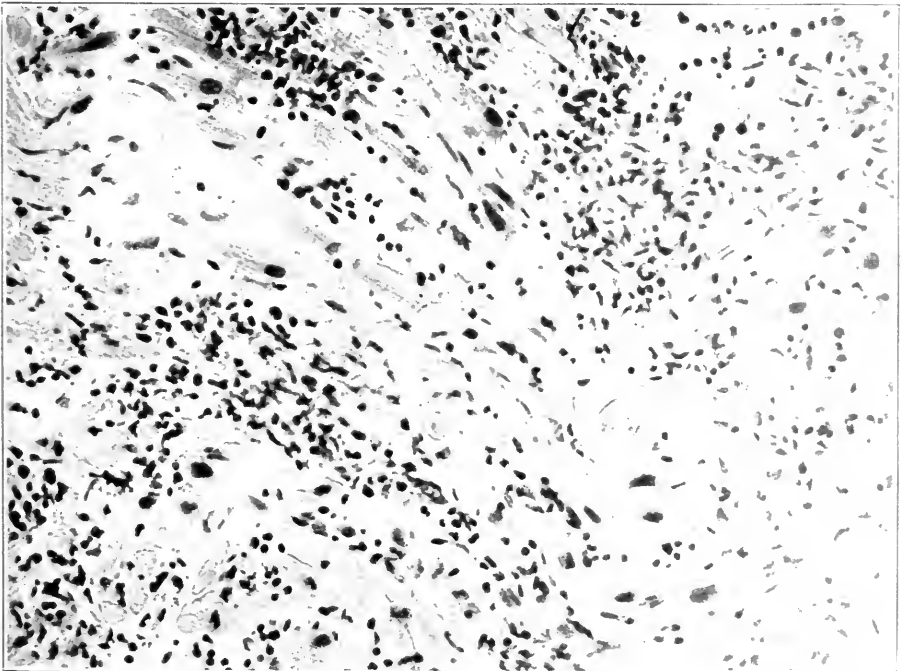


Fig. 4.—Chronic syphilitic myocarditis. Sudden death in middle-aged male with history of "cured" syphilis. More active process; plasma-cell infiltration more diffuse with larger focal infiltrations approaching miliary gummata. Abundant spirochetes.



and to focal reactions of lymphocyte and plasma-cell infiltrations would appear from our material to be less than that of the heart, aorta, and other tissues, but this impression may be due entirely to the smaller number of cases in which the central nervous system was examined, and to the more superficial study accorded it. The routine examinations reveal, at least one very important fact that such minute lesions as occur in other organs in syphilis are found also in the nervous system when no clinical symptoms of its involvement are present.

*Heart.*—The heart in every case showed microscopic lesions characteristic of spirochete localization; and in this organ more frequently than in any other has the spirochete itself been demonstrated by the Levaditi method. The cardiac lesions in the cases in which syphilitic infection was known to exist, and in those in which it was not suspected are identical. They vary greatly in degree. To the naked eye the hearts of the cases included in this autopsy material showed as a rule dilatation, hypertrophy, atrophy, and fibroid patches in the wall of the left ventricle. In many cases no fibroid changes were visible to the naked eye, and the occurrence of fibrosis and active infiltrations was determined only by the microscopic examination. The portion of the heart most frequently involved was the anterior wall of the left ventricle near the apex, the adjacent portion of the septum and the posterior left ventricular wall near the mitral ring. In cases of congenital infection the right ventricular wall may be chiefly affected. It must be emphasized that the determination of cardiac syphilis is essentially microscopic; when no myocardial changes can be seen by the eye the microscopic examination may reveal the most extensive lesions. This is especially true of the more acute and active cases.

The essential lesion of cardiac syphilis is an interstitial myocarditis characterized by infiltrations of lymphocytes and plasma cells along the vessels between the muscle fibers. These infiltrations are usually patchy or diffuse, very rarely focal or circumscribed, thus differing from streptococcus myocarditis. The infiltrations vary in degree, but usually are slight, the cells often being arranged in close single file between the fibers. To a superficial glance there appears to be only a slight increase of the interstitial nuclei. Polynuclears are few in the infiltrations, and eosinophiles are not present. The

cells of the infiltrations are probably chiefly histogenetic lymphocytes and young formative cells. Large epithelioid fibroblasts are very common, especially in the older, healing areas. Giant cells are rare. (See Figs. 1, 2 and 3.)

The entire heart wall from epicardium to endocardium, including the papillary muscles, may be involved in the infiltrations; but in the average case they lie nearer to the endocardium, often just beneath it, or in the middle layer of the myocardium. In acquired syphilis they rarely begin on the epicardial side, as they frequently do in congenital syphilis. In the most severe cases larger areas of infiltrations are grouped around the coronary arterioles. These may reach such a size as to suggest miliary gummata (see Fig. 4). Caseation, however, does not occur in these larger infiltrations. In two cases only were true gummata found in the myocardium. These were associated with the diffuse plasma-cell infiltrations.

In the more acute, severe and active cases the stroma of the infiltrated areas in the myocardium is edematous, often giving a slight reaction for mucin with specific dyes. In the older healed areas the stroma becomes fibroid and hyaline. In the great majority of cases the myocardium shows healed, fibroid areas in association with the active infiltrations (Figs. 5 to 8). In many cases the fibroid areas predominate, and search may be necessary to show the presence of active infiltrations. This is true especially of the older unrecognized cases. In every case, however, such active areas have been found, and no completely healed cases have been seen. A progressive fibrosis of the myocardium always takes place. In acquired syphilis the fibroid areas are always larger on the endocardial side; but in some cases they have extended completely through the myocardium. When this is the case, both endocardium and pericardium are thickened, and the latter usually shows a localized adhesion. These marked changes practically always occur just above the apex, in the anterior wall of the left ventricle; aneurysmal dilatation of the weakened wall at this point is not uncommon; rupture of the wall may take place as in two of our cases. More frequently, however, thrombosis occurs on the thickened endocardium overlying the fibroid patch, and death usually results from the progressive thrombosis of the left ventricle, or from embolism. In thirty of our cases thrombosis of the left ventricle over an area of syphi-



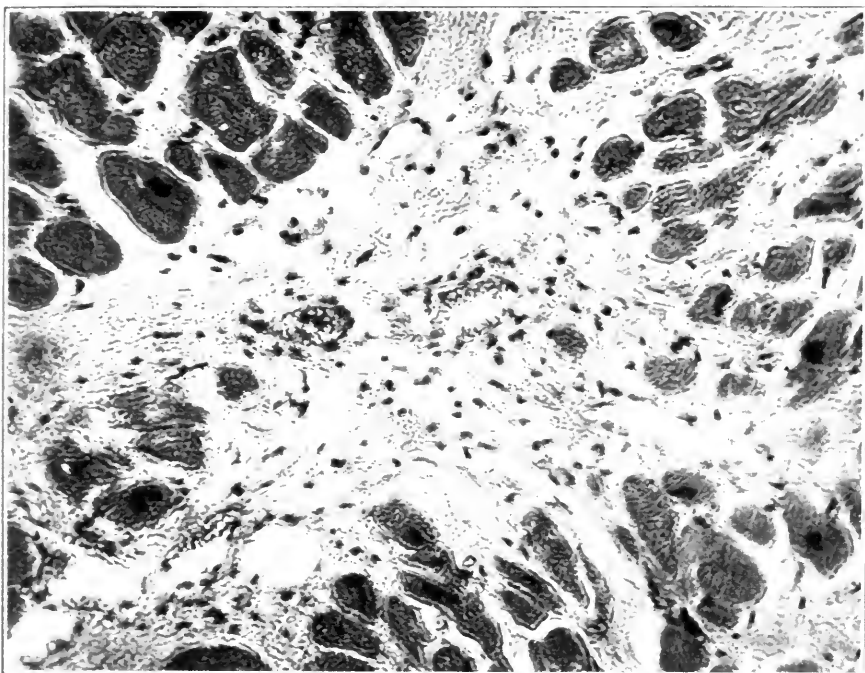


Fig. 5.—Chronic syphilitic myocarditis. Older process. Fibroid heart. Case of diabetes; unsuspected latent syphilis. Small active area in left ventricle wall in healing stage. Few spirochetes.

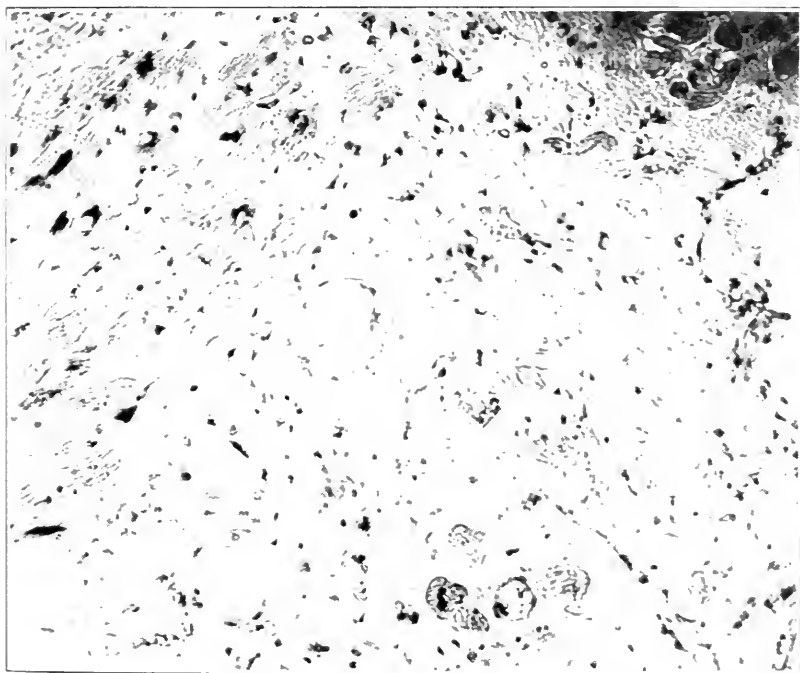


Fig. 6.—Chronic syphilitic myocarditis. Left ventricle wall from case of syphilis contracted 14 years previously. Suicide. Fibroid areas in heart with active plasma-cell infiltrations. Few spirochetes.



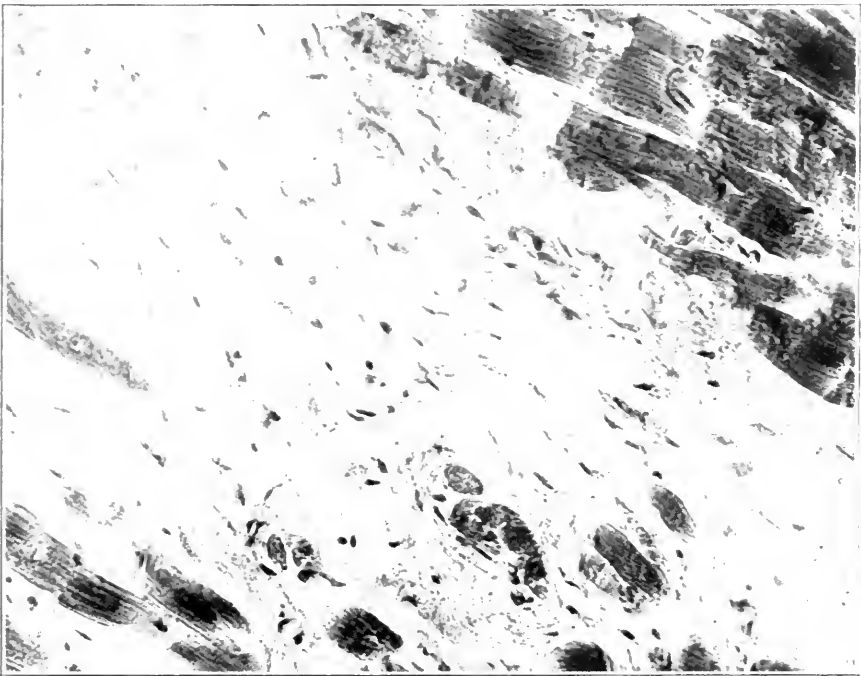


Fig. 7.—Chronic syphilitic myocarditis. Old "cured syphilis;" negative Wassermann; cardio-vascular-renal symptom-complex; dilated, fibroid heart. In area showing no more active plasma-cell infiltration than in photograph spirochetes found in small colonies.

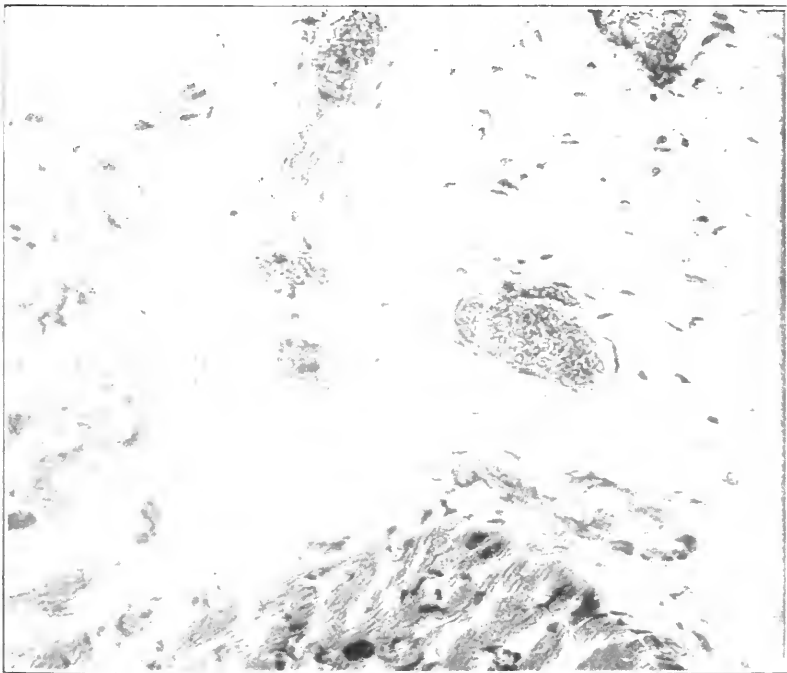


Fig. 8.—Chronic syphilitic myocarditis. Nearly healed fibroid area in left ventricle wall of old "cured syphilis." Slight plasma-cell infiltrations. Few spirochetes found after prolonged search.



litic infiltration or fibrosis of the ventricular wall was the cause of death. In the great majority of the cases of latent syphilis the left ventricle was dilated, and such dilatation was either the chief or an accessory cause of death. The "fibroid" heart is the ultimate outcome of all cases of latent syphilis. (See Figs. 7 to 11.)

In the congenital and active acquired cases spirochetes are fairly easily demonstrated between the heart muscle fibers. In the older cases, with fibrosis more or less well advanced, the demonstration of the spirochete becomes a task requiring patience and determination, spread often over days or weeks. They are, nevertheless, more easily found in the heart than in any other organ or tissue, so far as our experience goes. (See Figs. 12 to 15.)

The parietal and mitral endocardium appears resistant to the spirochete to a much greater degree than that of the aortic valves. In no case have I been able to demonstrate the occurrence of syphilitic changes in the mitral valves. Secondary streptococcus or staphylococcus endocarditis with mitral stenosis or insufficiency was in a number of cases, particularly those of congenital syphilis, the immediate cause of death. The heart of congenital syphilis seems to give a local predisposition to secondary infections. Sclerosis of the coronaries may or may not be associated with syphilitic myocarditis. In my material marked coronary sclerosis was rather a rare finding; the coronary involvement was perivascular rather than primarily vascular. Even in a number of the angina pectoris cases the coronary sclerosis, as far as the larger branches were concerned, was not marked, although these cases all showed marked fibrosis of the myocardium. Thrombosis of the coronaries was not observed in any case. The smaller terminal arterioles and capillaries are obliterated and destroyed by the perivascular infiltrations and proliferations, while the larger coronary branches rarely show much sclerosis, except in the cases showing a general arteriosclerosis. A striking feature of the fibroid areas is the dilatation of preexisting capillaries or veins or a new formation of such in the fibroid areas. Often such areas appear cavernous or sinusoidal, because of the large blood spaces present having practically no wall but that of the lining endothelium. These appearances are probably the result of a compensating circulation in newly formed capillaries. In younger scars the new formation of

capillaries is very striking, and this vascular proliferation appears to be one of the distinct features of syphilitic myocarditis.

The heart muscle itself in all of the cases presented varying degrees of hypertrophy with simple and brown atrophy, fatty degeneration, and necrosis, all of these changes usually being present in the same heart. In the immediate neighborhood or periphery of the infiltrations the heart muscle fibers often showed no changes at all; in other cases fibers extending through the lesions showed only hypertrophy. I have previously shown that colonies of spirochetes may be found in heart muscle appearing perfectly normal. While this is most common in cases of congenital syphilis, it is also found in late acquired syphilis. It is evident that the toxic action of such spirochetes upon the muscle fibers must be very slight indeed. The intensive study of these cardiac lesions tends to emphasize more and more the mild and slowly progressive nature of the latent syphilitic infection.

The clinical features of these heart lesions can not be presented in detail here, and for the present only generalizations can be given. While a history of symptoms is wanting in some cases, the great majority of the cases included in this material presented symptoms of cardiac weakness, and circulatory disturbances. A very large number of the cases were frankly those presenting the cardio-vascular-renal complex. The termination of the case was frequently cardiac dilatation. Shortness of breath, palpitation, precordial pains, anginal attacks, irregularity of pulse, swelling of ankles, dizziness, general weakness, ringing in ears, etc., were the most common subjective symptoms. All of our cases of angina pectoris were syphilitic. The blood pressure may be high or low; the cases are about evenly divided in this respect. The disturbances of rhythm are very prominent and of every variety; the most interesting cases studied in the Clinic of Internal Medicine coming to autopsy belong to this material. "Functional" murmurs were common. The final clinical picture in all was that of an insufficient heart—a heart that could not do its work properly. The majority died a cardiac death; as shown by the hypertrophy and dilatation of the heart, and the chronic passive congestion of lungs and other organs. The chief pathologic findings at autopsy were those of a myocardial insufficiency ("fibroid heart") without (in the great majority of cases) accompanying valvular lesions.

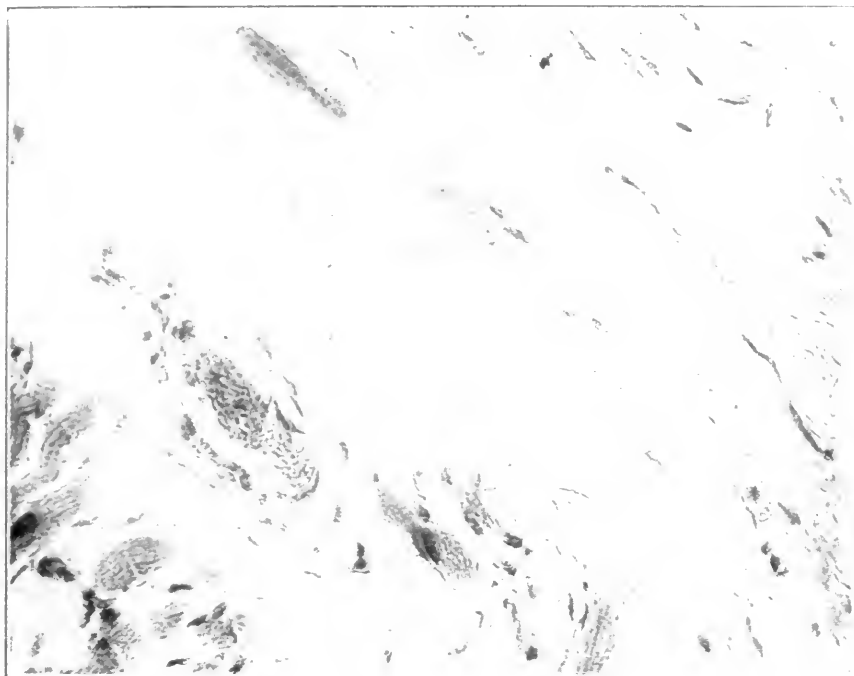


Fig. 9.—Chronic syphilitic myocarditis. Completely healed fibroid area. In such hyaline connective tissue without plasma-cell infiltration spirochetes have never been found.

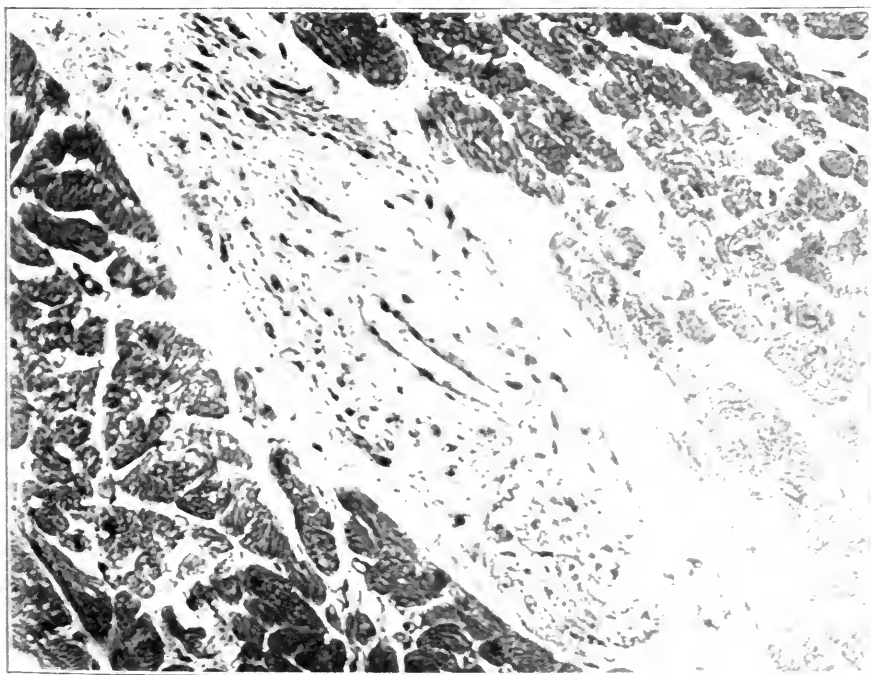


Fig. 10.—Tangential section of coronary vessel showing slight active syphilitic infiltration.





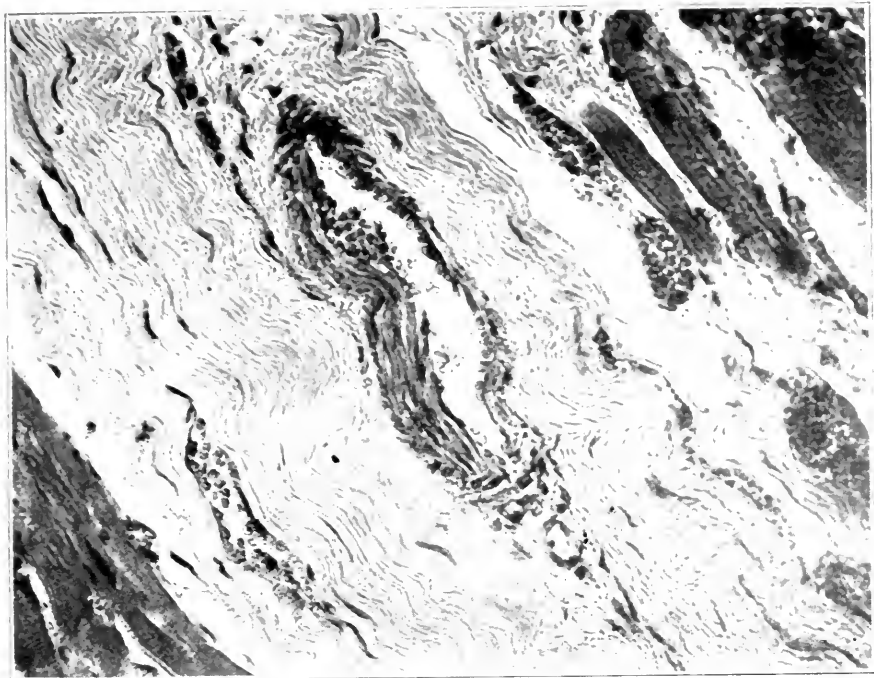


Fig. 11.—Similar section, from same case, showing complete healing: fibrosis without plasma cells.

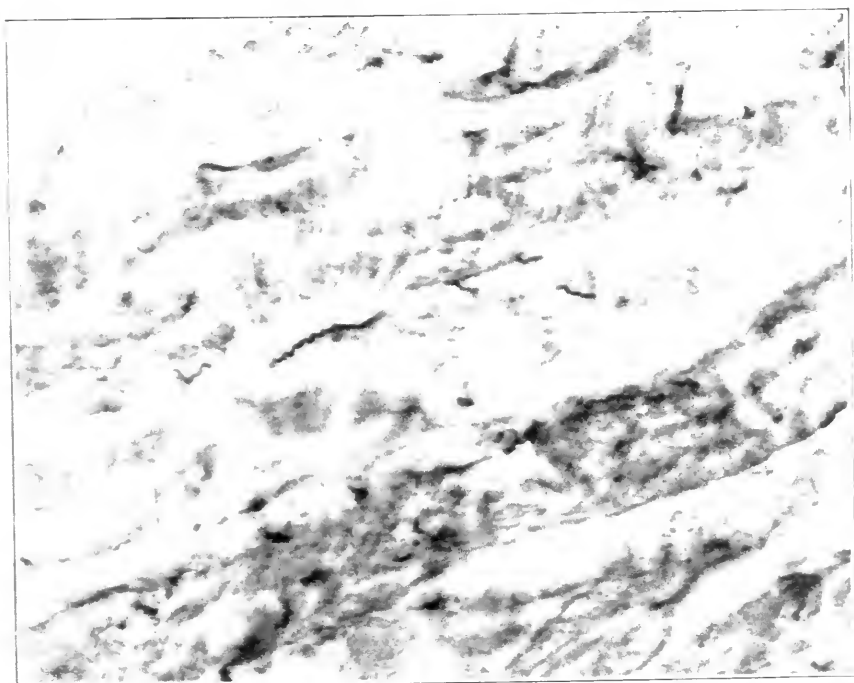


Fig. 12.—Levaditi preparation of active latent, unsuspected syphilis of left ventricle wall. Many spirochetes between muscle fibers.



**Aorta.**—The aorta, when examined microscopically, showed in every case of old syphilis characteristic syphilitic infiltrations in its media and adventitia. To the naked eye the changes may be very slight or marked. The gross appearances may be those of so-called senile atherosclerosis or of the type now generally recognized as syphilitic aortitis, or the two gross pictures were frequently combined in the same case, particularly in older patients. While the lesions in the majority of cases are most often seen in the beginning of the aorta and in its arch, they are often most marked in the abdominal aorta; and, in a few cases, were confined to this portion, so far as the gross appearances were concerned. The process is very common about the mouths of the aortic branches.

It is certain, from my experience, that the *gross appearances are no absolute criterion of the aortic condition*. When the gross appearances of syphilitic aortitis are present the pathologic diagnosis of syphilis may be given at the autopsy table without hesitation; but when the picture is that of atherosclerosis, no positive exclusion of syphilis can be made without a microscopic examination. The aorta may present no changes, or very slight ones, to the naked eye, but the microscopic investigation may show characteristic plasma cells along the vasa vasorum of the media and adventitia. This is true of all the early stages of the diseases. In the few cases of secondary syphilis examined at autopsy the aorta showed slight changes ("fatty degeneration of the intima"), or none at all, yet microscopic study showed extensive infiltrations along the vasa vasorum and around the small vessels in the prevertebral tissues. This is the early active stage when the demonstration of spirochetes can be most easily carried out. *The cases recognizable by the naked eye as syphilitic aortitis are old cases*; and the demonstration of the spirochetes in these becomes increasingly difficult. This is particularly true when to the syphilitic aortitis there are added the changes of atherosclerosis due to age or other etiologic factors. *In the great majority of old cases the gross appearances of atherosclerosis are combined with, and conceal those of syphilitic aortitis*. For this reason a negative diagnosis of syphilis of the aorta is of no value, in the absence of a thorough microscopic study.

The microscopic features of this form of aortitis are now so well known that they will be but briefly discussed here. Small infil-

trations of lymphocytes and plasma cells are found along the vasa vasorum of the media and adventitia, usually most marked around the vessels of the latter, and diminishing in degree as the vessel passes up into the media. Perivascular proliferation, fibrosis and obliteration of the small vessel then follows. (See Figs. 16 and 17.) The resulting disturbances of nutrition of the vessel wall are first seen in the intima and the inner portion of the media, in the form of fatty degeneration, atrophy and necrosis of the cells of this portion of the vessel, with weakening and thinning of the wall, followed later by fibrosis and hyaline change. The involvement of the media progresses steadily outwards, and because of the greater involvement of the media locally there results local thinning of the vessel wall and microscopic ruptures of the elastic fibers. Such changes naturally predispose to the development of aneurysms. In simple uncomplicated syphilitic aortitis the fibrosis of the intima is less than in atherosclerosis, and there is less tendency to secondary atheroma and calcification. The two forms of aortic disease are, however, combined in the majority of cases, and the microscopic picture presents the characteristics of both processes. In some cases the changes in the intima and media really represent a slow anemic infarction due to the shutting off of the blood supply as the result of the obliterative endarteritis in the arteries of the vasa vasorum in the adventitia. The obliterated arterioles often appear as concentric formations resembling tubercles, miliary gummata or even suggesting epithelial formations. The lymphocytic and plasma-cell infiltrations are in the early stages most marked in the perivascular lymph spaces of the arterioles; but later these infiltrations often become very marked around the greatly dilated veins. A new formation of capillaries is often seen in the adventitia and outer portion of the media. These infiltrations often are large enough to be regarded as miliary gummata, but the development of well-defined gummatous nodules with caseating centers and giant cells is rare. When these do occur they are usually multiple.

The demonstration of spirochetes requires much time and patient search. I have found them in the aorta of acquired cases of syphilis only in the perivascular infiltrations of the adventitia. They occur usually in small colonies. In congenital syphilis, however, the intima of the aorta may show localized proliferations and infiltra-



Fig. 13.—Levaditi preparation of chronic syphilitic myocarditis from case of unsuspected syphilis. Spirochetes at border of fibroid patch.

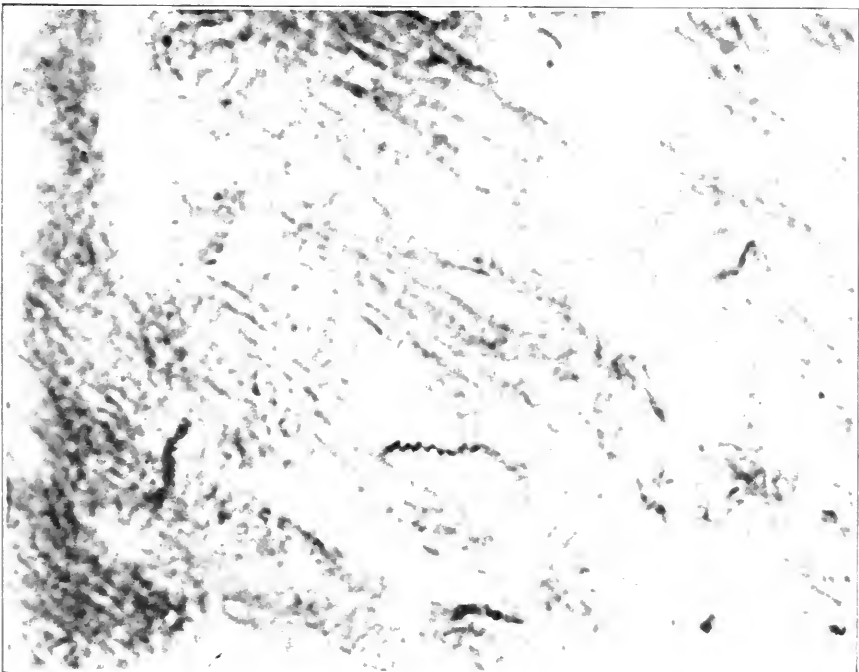


Fig. 14.—Levaditi preparation of chronic syphilitic myocarditis. Case of diabetes, syphilis not suspected, negative Wassermann. After prolonged search small colony of spirochetes found in small area of plasma cells at border of fibroid patch.





Fig. 15.—Levaditi preparation of fibroid heart from case of diabetes, with unsuspected syphilis, negative Wassermann. After six weeks search of blocks from left ventricle wall this colony of spirochetes was found at border of fibroid patch.

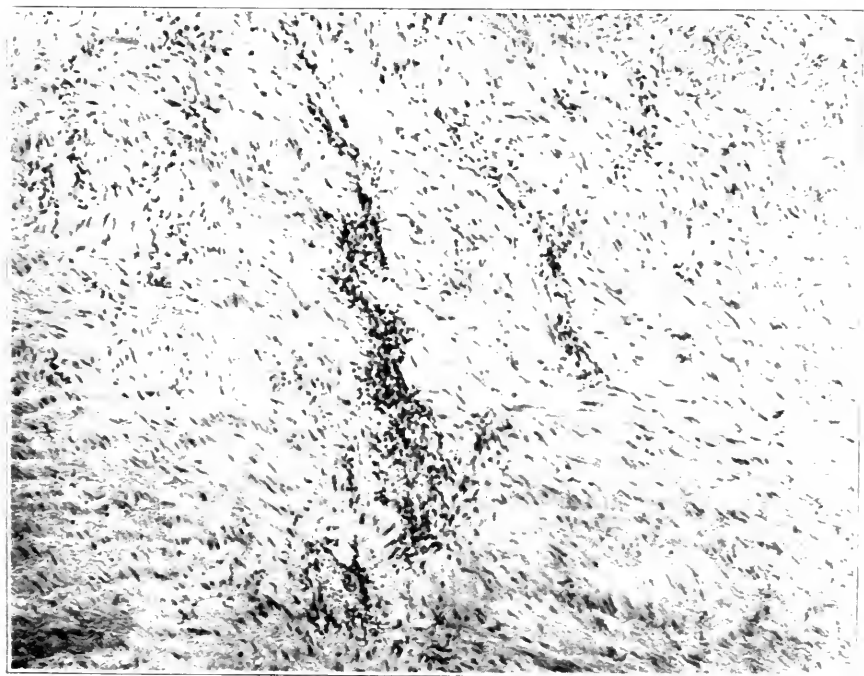


Fig. 16.—Typical syphilitic mesaortitis. All cases of latent syphilis show this lesion in the aorta wall; it is a practically constant sign of syphilis. Small plasma-cell infiltrations along the vasa vasorum, through the media of the aorta.





tions containing great numbers of spirochetes. In such congenital infections the syphilitic lesions of the intima may later heal and present the appearances of atherosclerosis. They then can not be distinguished from the local lesions of the intima found in typhoid fever and other infections.

*Pulmonary Artery.*—I have studied and reported a case of syphilitic aneurysm of the pulmonary artery with marked and characteristic syphilitic arteritis of this vessel and its branches. The presence of the spirochete was demonstrated in the aneurysmal sac, with blood clot in the wall. The organisms were found in very small numbers, possibly owing to the previous salvarsan treatment. The microscopic changes in the wall of the pulmonary artery were identical with those of syphilitic aortitis. How frequently such changes have occurred in the pulmonary artery in my cases I am unable to say, as no especial attention was paid to this vessel. In the microscopic notes on the lungs of these cases, there is frequent mention of thickened and hyaline pulmonary vessels; these changes were usually referred to the chronic passive congestion of the lung present in practically all cases. In but two other cases were there changes in the pulmonary artery so marked as to attract attention. One of these cases was that of a male who had had for some years a well-marked case of chronic cyanosis and polycythemia (Vaquez's disease). At autopsy his pulmonary arteries showed marked dilatation and atherosclerotic changes in the main branches with hyaline fibrosis and complete obstruction of many capillaries. The microscopic examination showed the presence of a typical syphilitic mesarteritis of the pulmonary arteries; and the polycythemia is explained as compensatory to the circulatory changes in the lung. This case undoubtedly falls into the group, of which a number have been reported from South America and India, of syphilis of the pulmonary arteries associated with polycythemia and cyanosis ("Ayerza's disease"). The other case of unusual atherosclerosis of the pulmonary artery showed microscopic changes of syphilitic arteritis without other complications.

*Syphilis of Peripheral Arteries.*—In several cases syphilitic arteritis of the femoral artery and its large branches, the popliteal and the tibial arteries was noted. In one case, a colored woman, the entire systemic arterial trunks and their smaller branches showed

severe syphilitic arteritis with multiple thromboses. The abdominal aorta from the level of the diaphragm down and all of its branches contained organizing thrombi; globular thrombi were present in all four chambers of the heart. This case presented a condition not described in the literature—a very active generalized syphilis of the entire arterial system and heart. In all of these cases of syphilis of the larger arteries, the microscopic picture is identical with that seen in syphilis of the aorta and pulmonary arteries. There is the same lymphocytic and plasma-cell infiltration along the vasa vasorum of the media and adventitia with localized degeneration and fibrosis of the intima and inner portion of the media. In the smaller branches the entire vessel wall is involved and the process takes on the character of a proliferative endarteritis, as in the case of the arterial vasorum. The clinical importance of these arterial changes in this autopsy material has been chiefly that of aneurysm, thrombosis, embolism, infarction and gangrene, in about 5 per cent of the total number of autopsies; in the remaining cases no definite clinical symptoms could be ascribed to the aortic changes beyond the general circulatory disturbances common to all of the syphilitic cases, and which have been interpreted as chiefly cardiac in origin.

*Pancreas.*—The pancreas in all of the old cases of syphilis showed a greater or less degree of atrophy and interstitial fibrosis. In the majority of cases the changes were irregularly scattered throughout the organ, the body and the tail portions showing an especial tendency to involvement. Lobules showing marked change may be surrounded by those showing no change. In other cases the entire pancreas showed a diffuse fibrosis, varying from slight to the most marked degree. The connective tissue increase is both inter- and intra-lobular. In the majority of cases it was old, containing few cells; but in two cases of diabetes it was more fibroblastic in character and contained many cells of lymphocyte and plasma-cell type. Careful search has revealed, however, in every case active areas of plasma-cell infiltration. These areas often show an edematous or myxomatous connective tissue, the plasma-cells and lymphocytes may be few or many. Such inflammatory areas are most often found at the border of a lobule, and the latter are invaded by new connective tissue from the periphery usually, although occasionally the

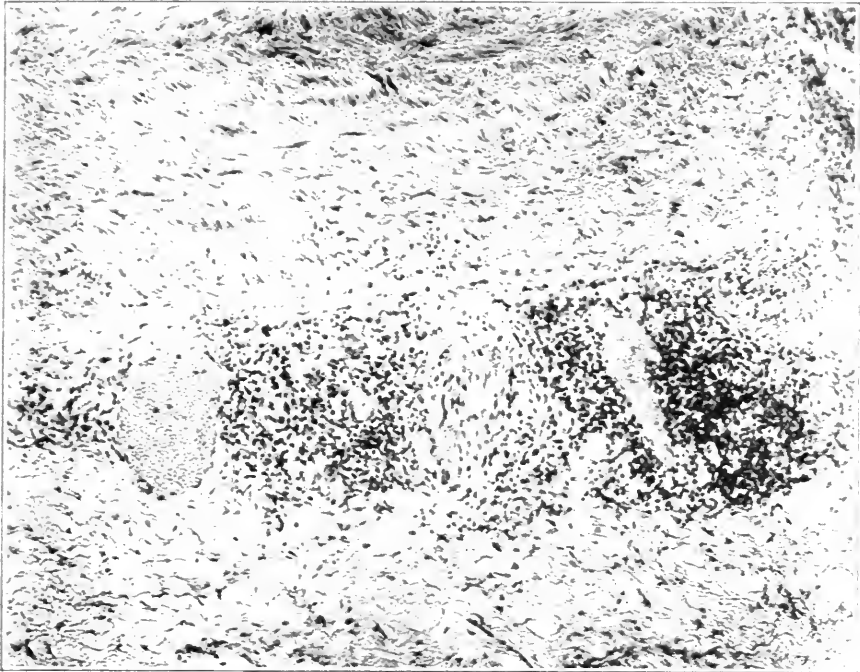


Fig. 17.—Portion of media and adventitia of aorta from case of latent, unsuspected syphilis. Characteristic plasma-cell infiltrations around the vasa vasorum, with obliteration of the small artery. One of the most constant and characteristic lesions of latent syphilis. Spirochetes are usually in small numbers and found only in these active foci.

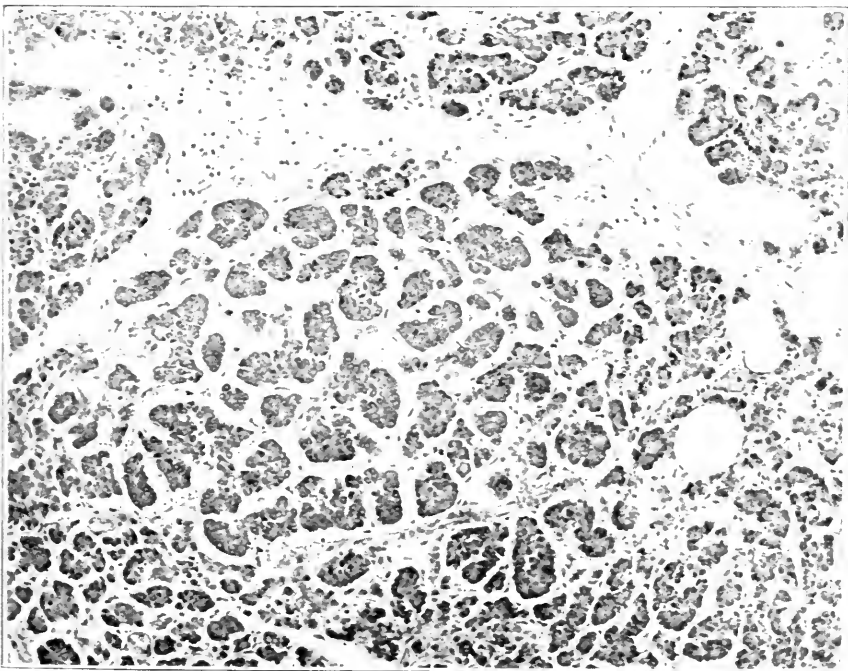


Fig. 18.—Pancreas from case of diabetes, with unsuspected syphilis and negative Wassermann. Diffuse chronic interstitial pancreatitis. Very small active areas, in which, small groups of spirochetes were found.



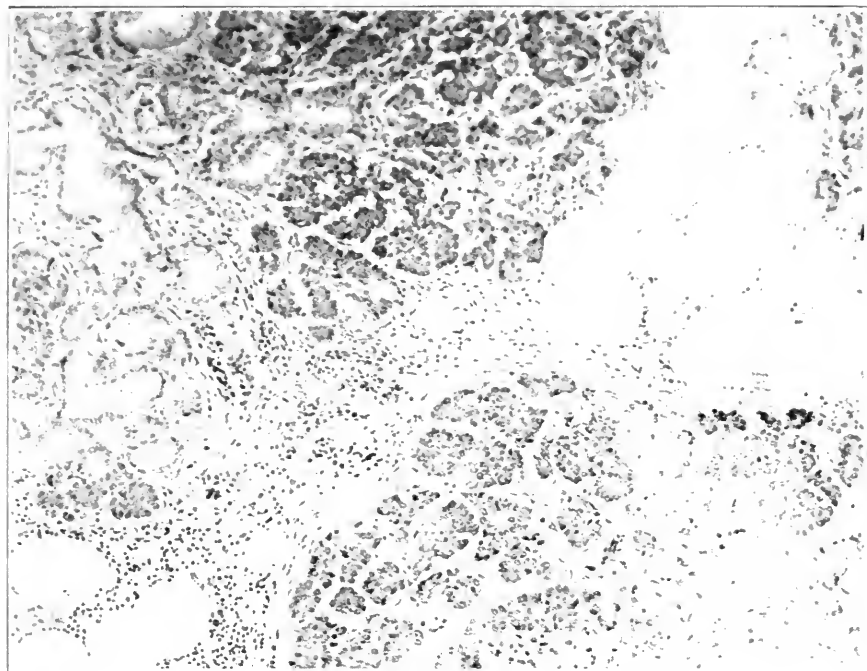


Fig. 19.—Chronic syphilitic pancreatitis, with active areas, from case of diabetes, unsuspected syphilis and negative Wassermann reaction. Spirochetes found in heart and pancreas.

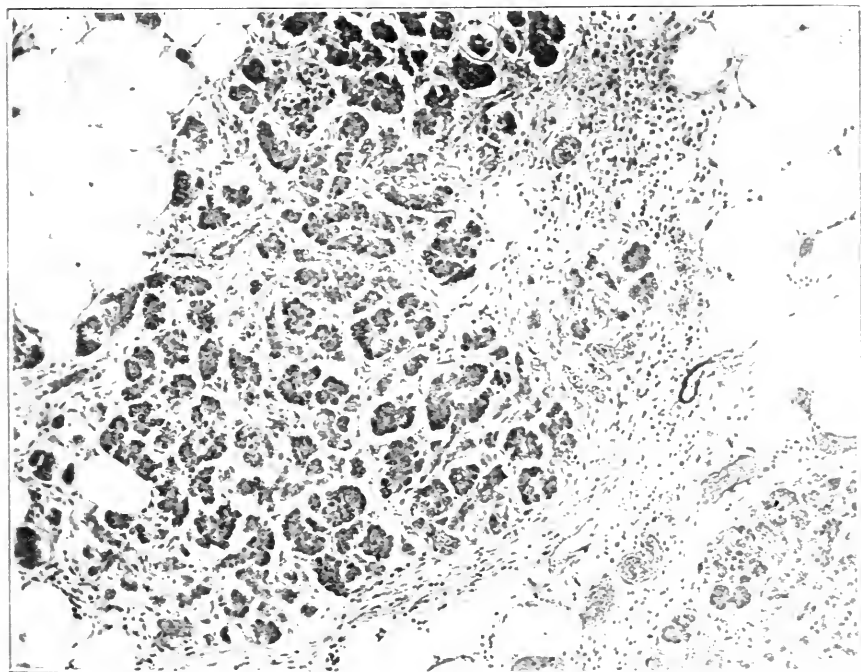


Fig. 20.—Chronic syphilitic pancreatitis. From tail of pancreas; same case as preceding.



process appears to begin within the lobule. Fibrosis of the islands in varying degrees is often associated with the interstitial inflammation. In all of the cases of diabetes but two, island fibrosis was very marked, and presented characteristic features, the chief of these being the thick crowding of large hyperchromatic cells around the border of the hyaline fibroid islands. These cells were interpreted as regenerative or hypertrophic. In several nondiabetic cases the chronic pancreatitis and fibrosis of the islands was as marked, or even more so, than in the diabetic cases.

The pancreatic acini show varying degrees of atrophy in the affected areas. As the acini disappear fat is deposited in the connective-tissue cells; in many cases such fatty infiltration following the atrophy of the pancreatic parenchyma is very marked. Islands completely surrounded by fat tissue are often seen in the tail portion of the organ. Regenerative formations may be found in practically every case; they often reach such a degree as to appear neoplastic, resembling adenomata or cystadenomata. The newly formed acini resemble islands and are undoubtedly often mistaken for newly formed ones. They arise from the epithelium of the lobular ducts and also from that of the larger ducts. Newly formed acini may even be found within dilated larger ducts. In every one of the cases of syphilis the pancreas showed evidences of progressive destruction and repair. No evidence of the new formation of islands, however, was ever seen. Sclerosis of the blood vessels of the organ may or may not be associated with the pancreatitis. Some degree of it was often found in the lobules showing marked interstitial change; but only in a relatively small number of cases was the inflammatory process associated with a general sclerosis of the pancreatic arteries. (See Figs. 18 to 26.)

As to the syphilitic nature of these lesions, they are identical with those produced by the spirochete in other tissues and organs. The localized plasma-cell infiltrations, slight fibroblastic proliferation, edematous or mucoid stroma, eventually fibrosis, are histologically specific characteristics, I believe; and in further proof of this view, spirochetes were demonstrated in these areas in the pancreas of two cases of diabetes.

So far as the clinical significance of these pancreatic changes is concerned the only fact of importance shown is their association with

diabetes. In eleven out of twelve cases of diabetes coming to autopsy, the heart, aorta, pancreas, adrenals, (testes, in the males) and other tissues showed the characteristic plasma-cell infiltrations and fibrosis of latent syphilis. In five cases *Spirochete pallida* was demonstrated in the myocardium, and in two cases (Fig. 27) in the pancreas itself. In the pancreas they occurred in small colonies in the areas of cell infiltrations. That diabetes is the result of syphilis I do not venture to assert. If it is true that a chronic interstitial pancreatitis is the most common pathologic finding in the pancreas in diabetes, it seems very likely that syphilis is the most common cause of interstitial pancreatitis, but not necessarily, of course, the only cause. Syphilitic pancreatitis may be a common cause of diabetes, if it can be shown that interstitial pancreatitis is the essential pathology of diabetes.

*Adrenals.*—Small infiltrations of plasma cells and lymphocytes are of constant occurrence in the adrenals of cases having known syphilis and unsuspected latent syphilis. In the great majority of cases these infiltrations are slight. They occur usually in the medullary portion or in the inner portion of the reticular zone of the cortex. (See Fig. 28.) They are usually perivascular. Fibroblastic proliferation of the stroma or fibrosis may or may not be present; the capsule of the organ is usually thickened, and perivascular infiltrations of small size occur in the surrounding tissues. The walls of the blood vessels usually are thickened. Very rarely the infiltrations are so marked as to assume the characters of miliary gummata. Caseating gummata with giant cells have not been seen. In three cases the syphilitic infiltrations and fibrosis were so marked as to have caused nearly complete atrophy of the greater part of the organ. All three of these cases presented the symptom complex of Addison's disease. In one of these cases marked syphilitic infiltrations occurred also in the adrenal and semilunar ganglia. With the exception of these three cases no symptoms were observed that could be directly ascribed to the syphilitic changes in the adrenals. Whether in the less severe cases disturbances of adrenal function may be responsible for the low blood pressure seen in some of the cases it is, of course, impossible to say. Another striking feature of the adrenals in chronic syphilis is the marked lipoidosis of the cortex seen in so many cases. This lipoidosis may be patchy, involving certain cir-



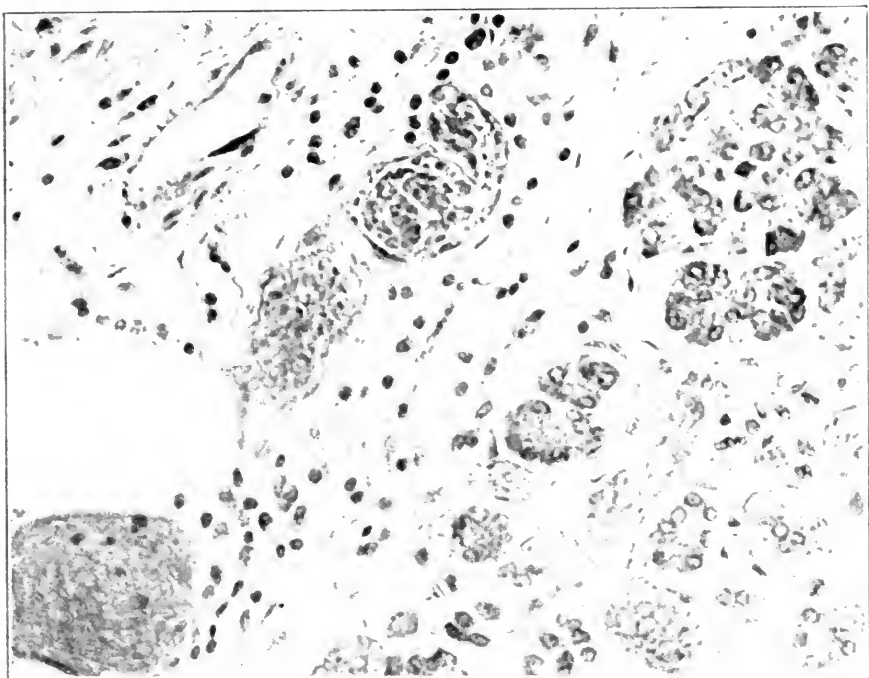


Fig. 21.—Chronic syphilitic pancreatitis. Higher power. Same case as preceding. plasma-cell infiltration; increase of stroma, and atrophy of acini.

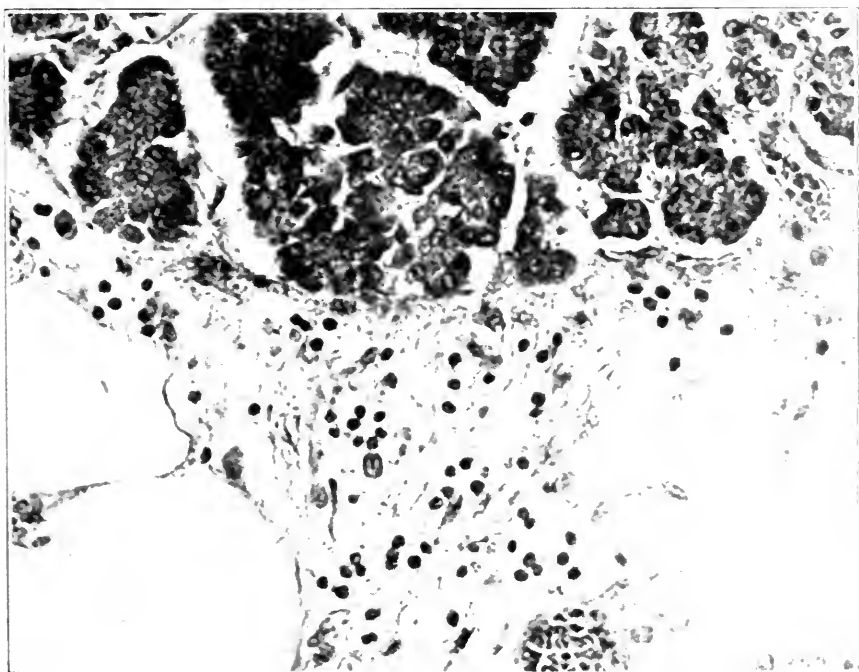


Fig. 22.—Chronic syphilitic pancreatitis. Same case as in Fig. 18. Small area of active plasma-cell infiltration and edema, in which spirochetes were found.



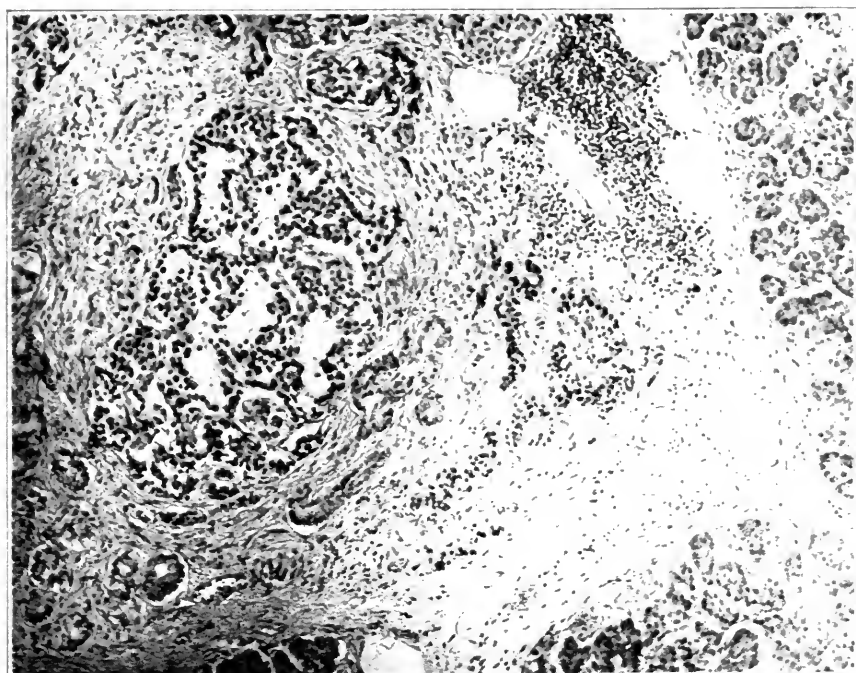


Fig. 23.—Chronic syphilitic pancreatitis. Same case, as in Figs. 19-21. Area of active syphilitic inflammation; new formation of pancreatic acini.

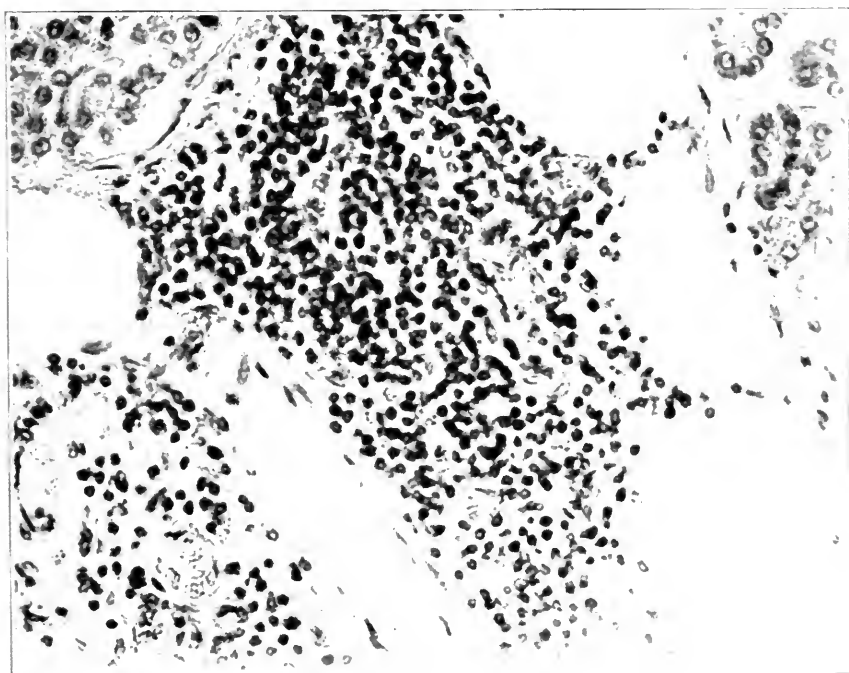


Fig. 24.—Chronic syphilitic pancreatitis. High power view of active area of plasma-cell infiltration seen in preceding.



cumscribed areas in the cortex, or it may involve the entire cortex. The cells are filled with numerous, large doubly refracting droplets that stain a brownish red with Sudan III and Scharlach R; with osmic acid many of the droplets take no stain, while others are grayish brown. The significance of this lipoidosis is not apparent, nor is its relation to syphilis. It is probably to be interpreted as an expression of a cholesterolemia or cholesterol retention, as a feature of a general disturbance of metabolism.

*Liver.*—The liver showed chronic passive congestion and atrophy (brown atrophy chiefly) in every case. Gummata were found in five cases, hepar lobatum in eight, atrophic cirrhosis in ten and an intra-lobular cirrhosis in one, Glissonian cirrhosis in three cases, while localized fibrosis was very common. The inflammatory lesions varied from slight plasma-cell infiltrations of the periportal tissue to the most marked cirrhotic changes. The relationship of these latter changes to syphilis has not been absolutely determined except in a few cases in which spirochetes were found in such infiltrations. It is worthy of note that in a case of secondary syphilis dying of salvarsan poisoning focal necroses containing spirochetes were present throughout the liver. (See Fig. 29.)

*Testis.*—In all of the male cases the testes showed varying degrees of atrophy and fibrosis. In the more active cases plasma-cell and lymphocyte infiltration between the tubules, fibroblastic proliferation of the stroma, thickening of the basement membrane and diminished spermatogenesis are the chief changes. (See Fig. 30.) These changes may involve the entire organ, or occur in small scattered patches. In the older cases the germinal epithelium of the tubules may be entirely lost, the tubules collapsed, and represented entirely by the hyaline thickened basement membrane which still keeps the shape of the tubule. The interstitial cells remain preserved, and in many cases appear hypertrophic. The stroma between the tubules is thickened and hyaline. (See Figs. 31 and 32.) In severe cases the entire testis becomes fibroid. Spirochetes can be demonstrated only in the active cellular infiltrations. So far as size, shape, and consistency are concerned, the gross appearances of the affected organs may seem to be normal. The clinical significance of these changes is a progressive loss of spermatogenesis and virility. Many of the patients had complained of premature loss of sexual desire.

*Other Lesions.*—Throughout the *prevertebral tissues, root of mesentery*, along the *radicles of the portal vein*, and in the *pelvic tissues* there constantly occur in the bodies of old syphilitics minute perivascular infiltrations of lymphocytes and plasma cells, associated with fibroblastic and angioblastic proliferations, eventually fibrosis, of a more or less marked degree. That the spirochete is associated with these minute lesions has been definitely proved. Therefore, in all cases in which these occur the possibility of spirochete localization must be considered. Such minute syphilitic inflammations may be widespread; they may be found in any tissue or organ.

*Lungs.*—The occurrence of syphilitic localization in the lungs was positively determined in three cases only, in which there were vascularized granulomatous areas, gummatous in character. No especial study has been made of this organ. In nearly every case the lungs showed chronic passive congestion and more or less marked induration or fibrosis. This has usually been interpreted as the result of the chronic passive congestion. As other writers have already pointed out, this fibrosis of the lungs may be directly the result of syphilis; but to what extent this has been true in this autopsy material I have not had time to determine. The question should, however, be taken up by investigators, as our knowledge of syphilis of the lung is very fragmentary and vague.

*Spleen.*—Chronic passive congestion, atrophy, and sclerosis of the splenic arterioles are the almost constant findings in the spleens of old syphilitics. Gummata were found in three cases; and these were the only positively determined instances of spirochete localization in this organ. This is also a field requiring investigation. I have been unable to extend my studies to this organ.

*Kidneys.*—Changes in the kidneys—chronic passive congestion, atrophy, infarctions, local and diffuse inflammations—were found in practically all kidneys coming from these cases. The proportion of cases of chronic parenchymatous nephritis is very striking. Out of the first forty-one cases of this material studied there were seventeen cases of acute, subacute and chronic parenchymatous nephritis, and three cases of interstitial nephritis. The relation of these conditions to the syphilitic infection is not apparent. I have never found spirochetes in the kidney, but they have been looked for in only a few cases. This is also a field demanding investigation.

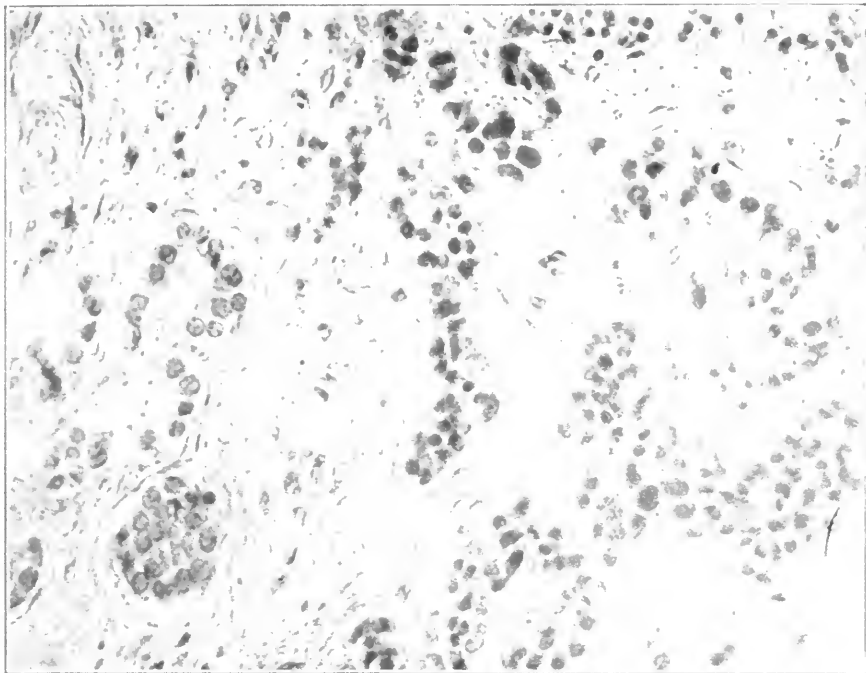


Fig. 25.—Chronic syphilitic pancreatitis. High power, showing fibroid stroma and atrophy of acini. Healed, inactive area.

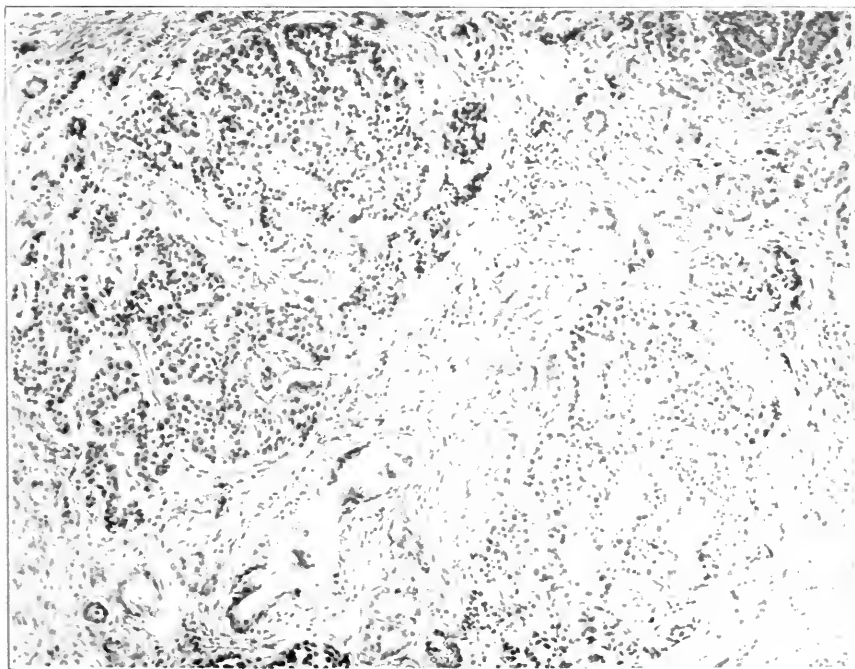


Fig. 26.—Chronic syphilitic pancreatitis. Area of severe change: fibrosis, destruction of pancreatic tissue and atypical regenerations of acini from pancreatic ducts. Such newly formed acini are usually mistaken for new islands of Langerhans.





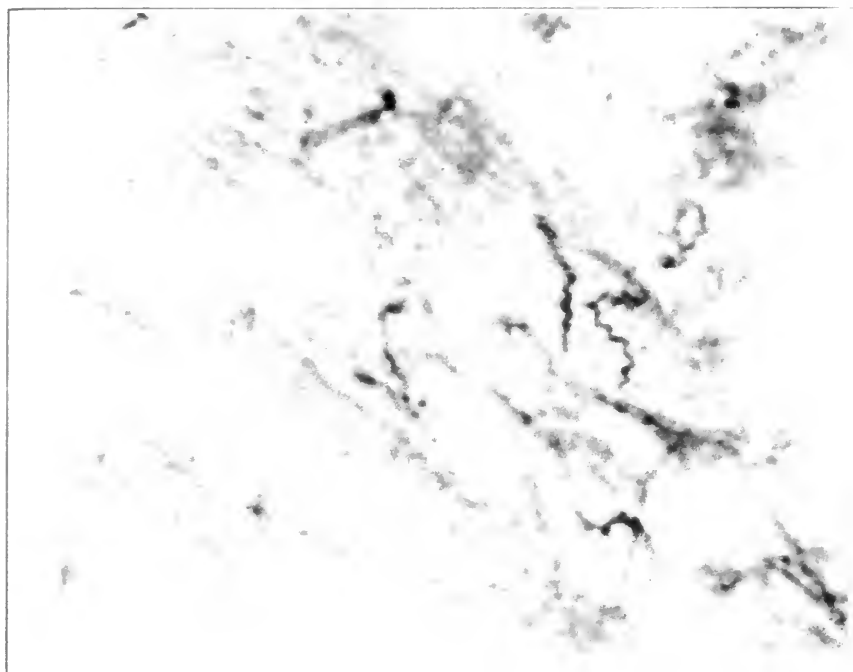


Fig. 27.—Colony of spirochetes in edematous, infiltrated area between lobules.

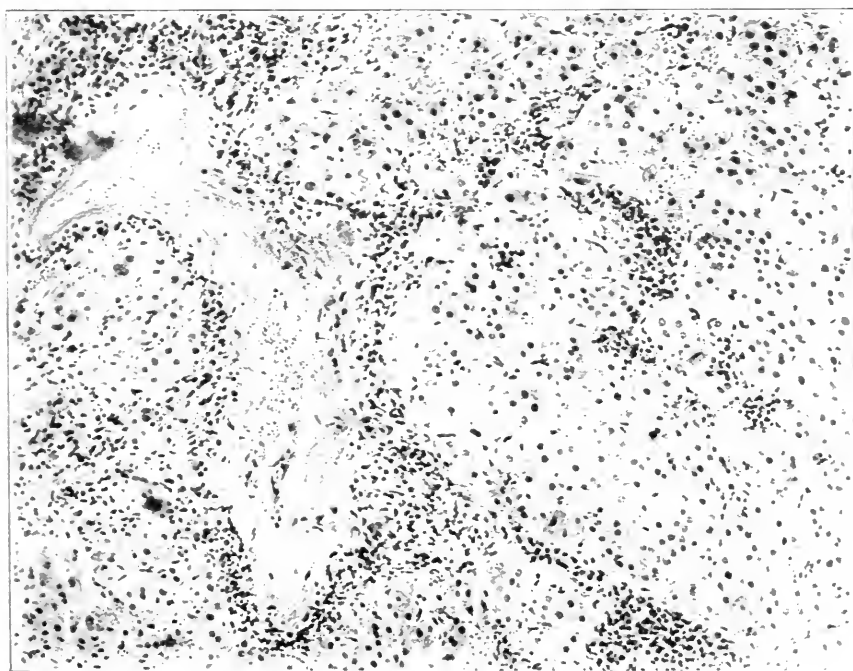


Fig. 28.—Syphilis of the adrenal. Plasma-cell infiltrations in inner zone of adrenal cortex and in medulla. One of the most constant findings in latent syphilis. These infiltrations are usually much less marked than in this case.



*Genital Apparatus.*—Outside of the testes spirochetes have been found in the sexual apparatus of the cases in this material once only, and that in the prostate of a young man with early tertiary syphilis clinically latent. Diffuse plasma-cell infiltrations occurred throughout the stroma of the organ, and not around the gland spaces as in chronic gonorrhea. The infiltrations were perivascular, interstitial, and not periglandular or subepithelial. Fibroblastic and angioblastic proliferations were prominent, and numerous giant cells occurred in the larger infiltrations, giving them the characters of miliary gummata without caseation. Groups of spirochetes were found in these. This case was the first one in which syphilitic lesions of the prostate were positively demonstrated. No spirochete study has been made of other portions of the internal reproductive tract in either sex.

*Lymph Nodes.*—The lymph nodes of the older cases of syphilis (even in young individuals) were atrophic and presented lymphoid atrophy, chronic sinus catarrh and hyaline formations (scars) in the germ centers and lymphoid tissue. In younger cases the nodes are frequently hyperplastic, but the germ centers, while enlarged, show a marked lymphocyte exhaustion. These appearances indicate a continuous demand made upon these organs against a persistent infection.

*Bone Marrow.*—Premature and excessive osteoporosis of the bones, and fatty atrophy of the marrow characterized the majority of cases. In a small number of cases the lymphoid marrow was found to be increased.

*Hemal Nodes.*—These were atrophic, in the great majority of cases. In association with marked anemia, and syphilis of the portal vein with Banti's disease complex, a marked hyperplasia of these nodes was seen, with great numbers of hemophages blocking the sinuses.

#### SUMMARY

The pathologic lesions, as described above are common to all cases of old syphilis (secondary stage onwards). They were found in known active cases of late syphilis (aortic aneurysm, gumma of brain and liver, tabes, paresis, etc.), in cases with history of syphilis treated and regarded as cured, in cases with negative and cases with positive Wassermann reaction; and, in the great majority of autopsies, in the bodies of those who gave no history of syphilis and no clinical signs or symptoms interpreted by the clinicians as indicat-

ing syphilis. It is probable that many of these patients never knew that they had syphilis; the infection in some cases is probably congenital, in others accidental. In other patients the previous infection may have been entirely forgotten or supposed to have been entirely cured. As syphilis is a "skin disease" to the average mind, both lay and medical, the symptoms predominating in this class of patients were not likely to arouse any suspicion of any relationship to the old infection, unless excited to such suspicions by direct and intensive questionings along this line, which they failed to receive.

It is, therefore, evident that syphilis as a latent infection is very much commoner than is generally supposed; and that the proportion of syphilitics in our ailing class is very high. It is, perhaps, idle to estimate the number of cases of syphilis in our population. To my mind the estimates of 5 to 15 per cent given by various writers are all too low; we would place the incidence of syphilitic infection in this country as nearer 30 per cent. An analysis of our vital statistics will easily show that at a very low estimate about one-tenth of all the deaths occurring in the United States can be attributed to syphilis. Dr. Osler has recently made a similar estimate for Great Britain. Syphilis is the leading infection and the chief cause of death, even when estimates are based upon our incomplete and imperfect knowledge of the pathology and symptomatology of the disease after the chancre and skin-symptom stages have been passed through. Death is rare in the first two years after infection with syphilis; the incidence of syphilitic death increases progressively with the years after the infection. Syphilis is particularly the cause of death in males between forty and sixty years of age; and as its symptomatology at this stage is in the great majority of cases either myocardial, vascular, renal, hepatic, etc., it is not recognized clinically as syphilis.

It is, further, very evident that infection with syphilis means *spirochete-carrying* in many, if not in all cases. The cases in the material analyzed in this study represent "*spirochete carriers*," and the pathology given above is the pathology of a mild latent infection in which there is but little antagonism between the infecting organism and its host. Syphilis after a preliminary invasion and disturbance of the body tends in the great majority of cases prob-

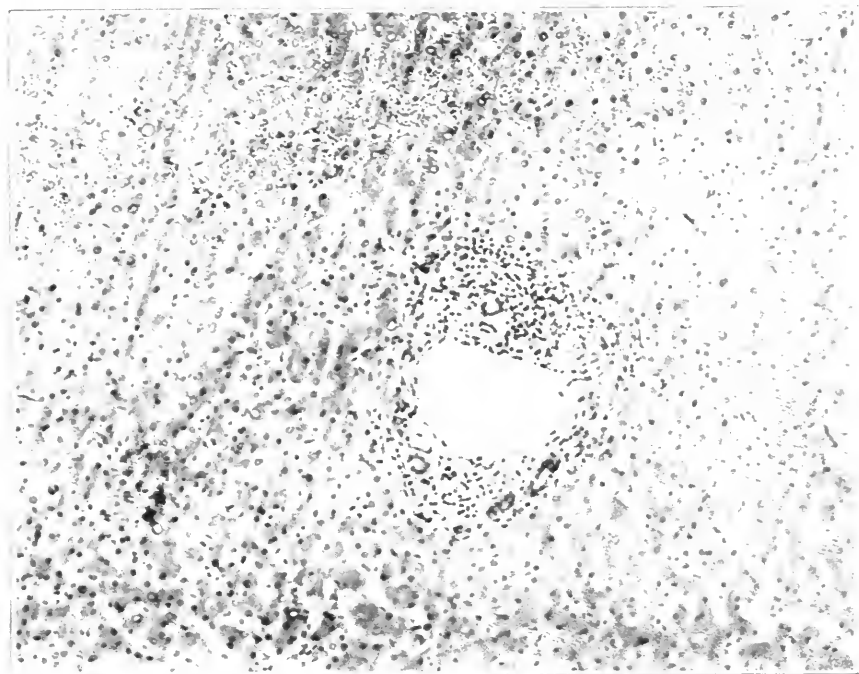


Fig. 22.—Liver from case of latent syphilis. The most constant and the mildest syphilitic lesion of this organ. Slight plasma-cell infiltration of portal tissues. Every degree from this very slight lesion, up to the most severe grades of cirrhosis presents itself in syphilis.



Fig. 30.—Active syphilitic orchitis. A constant lesion in all old cases of latent syphilis. Varies greatly in degree and extent. Spirochetes found only in active areas, as in this case.



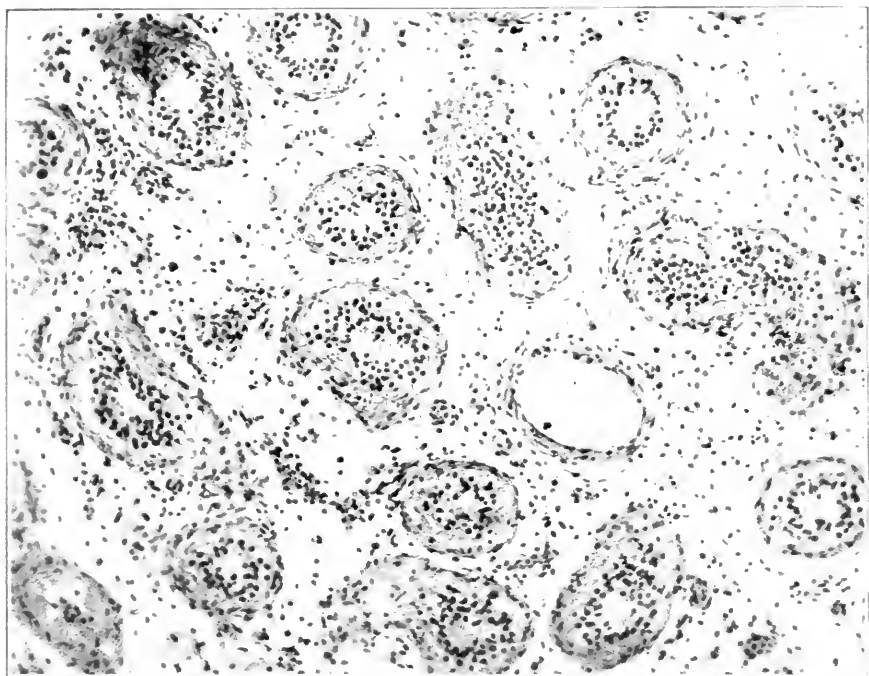


Fig. 31.—Subacute syphilitic orchitis. Increase of stroma; atrophy of germ cells; hyaline thickening of basement membrane of tubules; active syphilitic infiltrations. From case of congenital syphilis. Patient, aged 19 years.

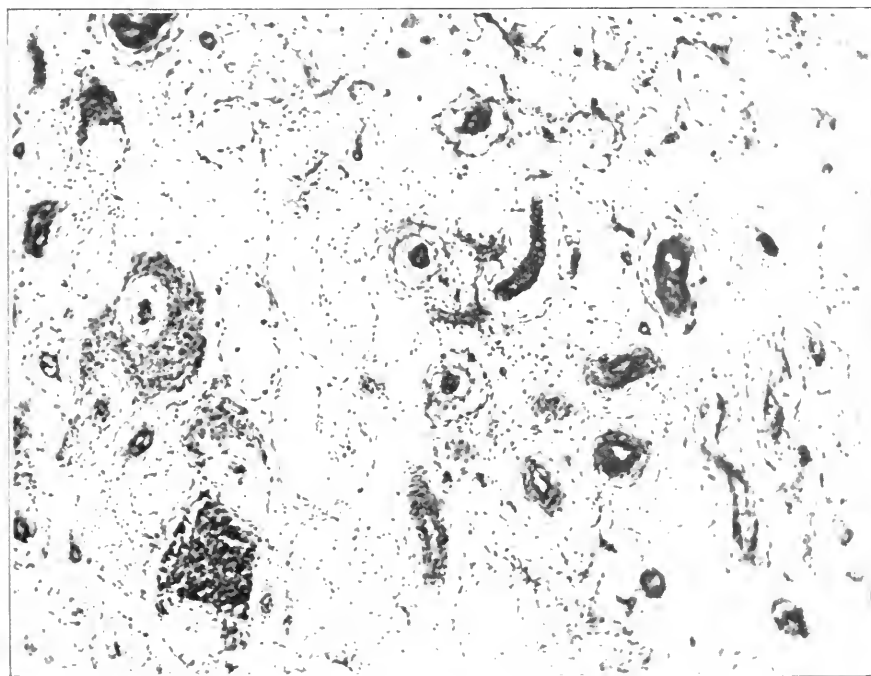


Fig. 32.—Chronic syphilitic orchitis. Complete fibrosis of testis, hypertrophy of interstitial cells. From same case as Fig. 31.





ably to become an infection not much more active or injurious than the streptococci of the mouth cavity. The very slight lesions found in so many cases prove this point beyond dispute. In women, particularly, does the infection often become so mild as to be practically nonexistent, except when pregnancy occurs and there is born a syphilitic child, or a syphilitic abortion or stillbirth occurs, with spirochetes in placenta, fetus, or child. *The spirochete carrier is immune to new infection only as long as he carries spirochetes.* This axiom we accept today, but we are yet far from understanding the reactions between the host body and the parasite spirochete. The individual tissue immunities and susceptibilities that undoubtedly exist, the reawakening of virulence on the part of the quiescent organism, its relationship to the Wassermann reaction, the question of positive cure, etc., are chief among the unsolved problems connected with this most important of all infections.

As to curability, I have never seen pathologically a cured case of syphilis. In all cases examined at autopsy active areas of specific inflammation are always seen, and such areas mean always the persistence of the spirochete. Perhaps these intratissue parasites should in cases without symptoms and negative Wassermann reaction be regarded in the same light as that in which we look upon the streptococci of the mouth cavity. Does the spirochete cease to be a cause of disease, and the body become a carrier of relatively or even quite completely harmless organisms? That some progressive injury is being caused is demonstrated conclusively by these studies. Immunity to the *Spirochete pallida*, and probably to all other organisms that enter the body tissues or, perhaps, even its passages and cavities, is paid for with a price—the price of defense. The infiltrations of lymphocytes and plasma cells in themselves may cause damage—infinitesimal, perhaps—but when persistent over a period of years may finally produce functional disturbances. The persistent slight damage and necessary repair by fibroblastic proliferation and the eventual fibrosis explains the latent period of syphilis and the final outcome in such terminal conditions as aortitis, myocarditis, pancreatitis, etc. The majority of cases of syphilitic infection die from the results of these slow mild inflammatory processes in the viscera and blood vessels rather than from paresis or

tabes. I am convinced that the great majority of all cases infected with syphilis die of *chronic myocarditis*.

The syphilitic is pathologically "damaged goods;" and the damage is a progressive one. He wears out sooner, his viscera more quickly reach their histogenetic limits, he actually becomes prematurely old, and there is a constant strain upon his defensive powers. All of these are arguments for the prevention of syphilitic infection rather than for its cure. No man can acquire syphilis, become clinically cured, which as far as we know means latency of the infection, that is, spirochete carrying, and have the same potential body-value and expectancy of life as before the infection.

This pathologic conception of the syphilitic, as probably always a spirochete carrier once the infection is acquired, should influence the therapeutic management of this chronic infection. The syphilitic, even when apparently perfectly well, should have his life laid out for him along lines tending to prevent the reawakening of the virulence of the organism or an increased susceptibility of the body tissues and organs. This is done for the patient who has once had clinical tuberculosis; when properly treated his future life is planned to prevent the reawakening of his infection, because he, too, is usually, if not always, still a carrier of the infective agent. But in the case of the syphilitic such hygienic measures are not applied, implicit reliance is usually placed upon a certain amount of salvarsan or mercurial treatment, while the infected individual is permitted to take up his life again as if he were an ordinary individual, and, as a rule, he succumbs prematurely to the stress and strains incident even to ordinary living. The treatment of syphilis, as it is ordinarily carried out, looks only to the present moment; it should look to the whole future life of the infected individual.

Syphilis in the woman presents peculiar problems. In the great majority of women infected with this disease it runs an absolutely latent course; the lesions at autopsy in the heart and aorta are always, except in rare cases, much milder than in man. Such women die of secondary infections or other conditions, rather than of myocarditis or aortitis. The pancreas and adrenals are, however, affected to the same degree as in man, the adrenals perhaps more so. A syphilitic woman may, however, pass her entire life without any clinical manifestations of syphilis, except the produc-

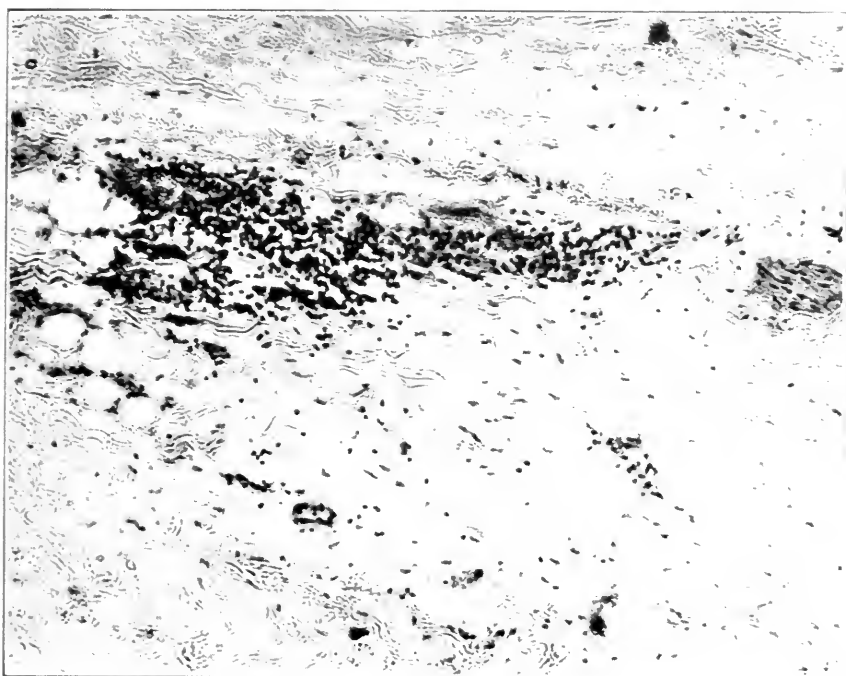


Fig. 33.—Syphilitic infiltrations in prevertebral tissues. Common findings in all old latent cases.

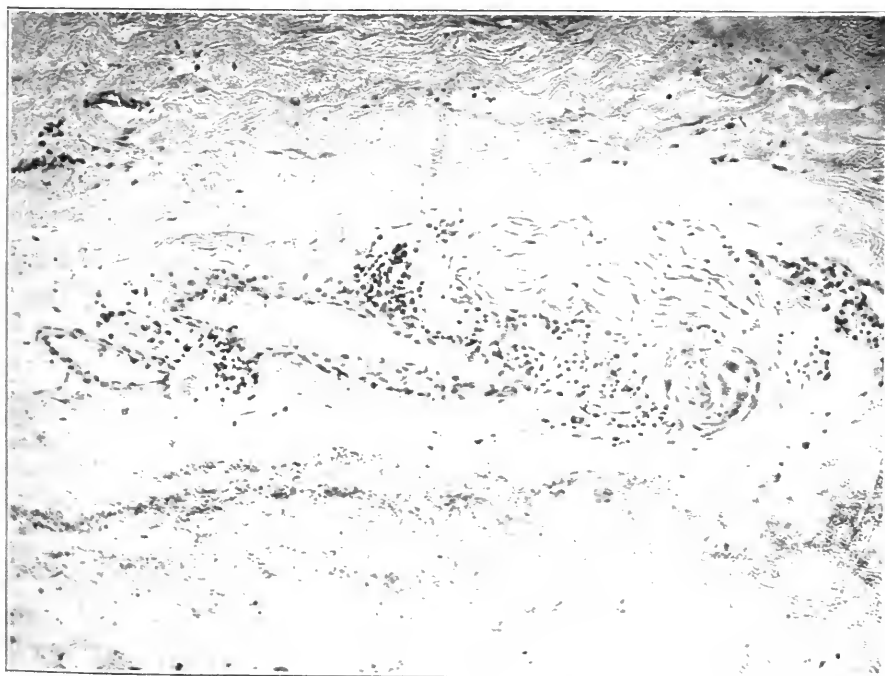


Fig. 34.—Small syphilitic infiltrations of plasma-cells around nerve trunk and vessels in root of mesentery. These are common in all old cases of active latent syphilis and are found particularly near the abdominal aorta and solar plexus.



tion of syphilitic progeny. I have come into touch with numerous examples of this kind, of which a few may be cited here.

1. Wife of a school teacher gave birth to a dead child. Autopsy of the infant revealed syphilis of the liver, and spirochetes. Both father and mother were above suspicion, absolutely negative histories, no signs, repeated Wassermanns of both negative. Pathologic diagnosis of syphilis not accepted by clinicians. Woman without treatment was allowed to become pregnant again and in a little over a year was again delivered of a dead and macerated fetus showing syphilis of liver and heart, and spirochetes. Repeated Wassermanns of both father and mother were negative. The only explanation of this case that could be obtained was in the fact that the father of the mother had been a chronic drunkard since youth.

2. Case similar to above. Two syphilitic children from father and mother, both apparently healthy, no history and no signs of syphilis, negative Wassermann in both. Father of mother a chronic drunkard since early manhood.

3. Father and mother apparently healthy, no signs and no history of infection, negative Wassermann in both, repeated abortions, one living child dying a few months after birth of congenital syphilis of liver, spleen and heart. The history of this case brought out the fact that the mother's father had been a chronic drunkard, "a beast," and diseased. Mother as a very young child had been rescued from the family conditions and brought up by a relative. A sister left behind became a keeper of a house of ill fame.

4. Grandfather on both sides a chronic drunkard. Father and mother apparently well, no signs of syphilis, negative Wassermanns in both. Three apparently healthy children, although minute examination reveals certain stigmata in bone development, then a child dying of active syphilis, then two more children apparently well, then a dead dropical fetus showing a marked syphilitic placenta.

5. Father a preacher, no history or signs of syphilis, negative Wassermann; mother's father had "blood poisoning," mother herself apparently well, negative Wassermanns repeatedly. Three syphilitic miscarriages.

It is very probable that in each of these cases the mother had congenital syphilis from her father. When there is a history of chronic alcoholism, syphilis is almost invariably present too. I believe that congenital syphilis in the woman is particularly likely to run a mild latent course without clinical manifestations, but that during the early months of pregnancy the spirochetes gaining entrance to the fetal circulation may regain their virulency and cause abortion, miscarriage, stillbirth or give rise to active clinical syphilis in children born alive. Such children may show the infection at birth or later.

It is very difficult to demonstrate spirochetes in the placentas of syphilitic children born at or near full term. In the fibroid villi they can not be found. In the young, myxomatous hyperplastic

villi of the syphilitic abortion occurring in the early months of pregnancy they are demonstrated more easily. I have found syphilitic lesions and spirochetes in placenta and tissues of a dead macerated fetus coming from a mother thoroughly treated with salvarsan according to modern methods, said by an expert in syphilology to be cured, and told that she might have healthy children. The first child was a syphilitic. It is also of interest to note the apparent fact that the tissues of the macerated fetus appear to be a good culture medium for the spirochete.

The constant occurrence of syphilitic lesions in the testes of latent syphilitics throws light upon the clinical facts, already known, that such cases may transmit the disease, and show spirochetes in their semen. The pathologic findings warrant the assertion that any individual who has had syphilis is particularly likely to pass out spirochetes in the semen and cause a seminal infection of woman or child. The localization of the spirochetes in the basement membrane of the seminiferous tubules makes this form of transmission practically a certainty. It is very probable that the great majority of cases of congenital syphilis are seminal infections of the mother and placental infections of the fetus.

So far as the Wassermann reaction is concerned I believe that a well-marked positive reaction indicates syphilis, with very few exceptions, such as generalized carcinomatosis, sarcomatosis, etc. In these conditions a 4-plus reaction may be found without any autopsy signs of syphilis. A negative reaction can not be taken as indicating the absence of syphilitic infection, nor can repeated negative reactions. I have repeatedly found active lesions of syphilis with spirochetes present when the reaction was negative. This is particularly true of gumma of the brain and congenital syphilis. As has been frequently noted the blood reaction is frequently negative in brain and cord syphilis when that of the spinal fluid is positive. I have had an opportunity of examining the bodies of eight cases dying from salvarsan poisoning; three of these were children with congenital syphilis, and of the five adult cases, three had syphilis of the central nervous system and had intradural treatments. In the congenital cases the treatment apparently had not in the slightest degree affected the number of spirochetes. In two of these cases the tissues throughout the body were swarming with

spirochetes. In an adult case with secondary lesions the liver contained multiple focal necroses with spirochetes present in the necrotic areas. It is a question as to whether these focal necroses were due to the spirochetes primarily or to the action of the arsenic. In all cases death was apparently due to the toxic action upon the renal epithelium.

#### CONCLUSIONS

1. The gumma is not the essential typical lesion of old or latent syphilis. It is a relatively rare formation; and the great majority of cases of syphilis run their course without the formation of gummatous granulomata.

2. The new pathology of syphilis is based upon the demonstration that the essential tissue-lesion of either late or latent syphilis is an irritative or inflammatory process, usually mild in degree, characterized by lymphocytic and plasma-cell infiltrations in the stroma particularly about the blood vessels and lymphatics, slight tissue proliferations, eventually fibrosis, and atrophy or degeneration of the parenchyma.

3. These mild inflammatory reactions are due to the localizations in the tissues of relatively avirulent spirochetes.

4. Syphilitic inflammations of this type occur in all tissues and organs; but are most easily recognized in the nervous system, heart, aorta, pancreas, adrenals, and testes. They are, however, usually widely distributed throughout the entire body, although in individual cases showing especial predilection for certain organs or tissues. No explanation of these system, organ, or tissue predilections is yet evident; neither is there any explanation of those cases in which all organs and tissues show the most severe degree of these lesions.

5. The syphilitic is a spirochete carrier. In this respect, the *Spirochete pallida* is to be classed with the trypanosome, the malarial organisms, lepra and tubercle bacilli, streptococcus, etc.

6. Syphilis tends to become a mild process; but at any time the partnership between the body and the spirochete may become disturbed, and tissue susceptibility or virulence of the spirochete become increased so that the disease again appears above the clinical horizon.

7. Immunity in syphilis depends upon the carrying of the spiro-

chete. A price is paid for this immunity in the form of the defensive inflammatory lesions previously described.

8. The disastrous effects of syphilitic infection usually require a period of years for their development. The slowly progressive lesions, fibrosis and atrophy, may at last manifest themselves in paresis, tabes, myocarditis, aortitis, aneurysm, diabetes, hepatitis, or in many other forms of tissue damage and functional disturbance. Lesions of the viscera are much more common and important clinically than those of the central nervous system, but they are rarely recognized as syphilitic by the clinician. Syphilitic death occurs most frequently in males between the ages of forty and sixty. Chronic myocarditis is the most common form of death due to syphilis.

9. The pathologic diagnosis of syphilis is essentially microscopic. Only in a relatively small number of cases are the gross lesions (tabes, gumma, aortitis, etc.) typical enough to be recognized by the naked eye. A negative diagnosis of syphilis can not be given with any certainty without a routine microscopic examination of all organs and tissues, but particularly of the left ventricle wall, the aorta, both its arch and abdominal portion, the testes, pancreas, and adrenals.

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# DEGENERATIVE CHOREA (HUNTINGTON'S TYPE) WITH THE SEROLOGY OF GENERAL PARESIS\*

REPORT OF TWO CASES: ONE WITH AUTOPSY

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IN a previous article, written on Danvers Hospital material, one of us (Lowrey<sup>1</sup>) has made a clinical report of Case 1, which has also been included in Southard and Solomon's book on *Neurosyphilis* (Case No. 72). Since these reports have appeared, the patient has died, and an autopsy was performed by the junior author. The second case has recently been observed at the Psychopathic Hospital, and shows a number of very interesting features aside from the unusual combination of chorea and paresis.

Neither of these cases is justifiably to be regarded as Huntington's chorea. In neither case do we have any *family history of chorea associated with dementia coming on in adult life*, and these are the requisites for the establishment of the diagnosis; hence we speak of them as "degenerative chorea (Huntington type)," meaning thereby a chorea clinically resembling Huntington's chorea, but without a family history.

Typical cases of Huntington's chorea do not show spinal fluid changes, nor is the pathology of the condition at all clear. Such findings as have been recorded—atrophies, meningeal thickenings, etc.—are not characteristic, but common to a number of nervous and mental conditions of adult and advanced life. Rather should we look to the *locus of the lesion* for an explanation of the symptoms. The basal ganglia have been under suspicion as the locus of disease

\*Danvers State Hospital Contribution (No. 65) and Psychopathic Hospital Contribution, Series of 1918.

responsible for the choreic movements, and certain unpublished work of which we have knowledge appears to prove this point. Unfortunately, the lesions in our autopsied case are so widespread that we are not able to offer any conclusive evidence on pathologic locus.

That choreatic movements may occur in paresis is well known, but receives very little attention. Kraepelin says in his textbook (Vol. II, p. 358), "Also choreatic movements can occur (in paresis). If they precede for a long time the outbreak of the disease, the possibility of Huntington's chorea has to be considered." This is all that we can find in the book about this association. Spielmeier, in Lewandosky's *Handbuch der Neurologie*, (Vol. 3, p. 499), says, "Many paretics show a very marked trembling of a coarse, irregular character, that often goes over into a kind of shaking. This shaking and the spreading of the motions appears occasionally like the motion of Huntington's chorea." Nonne devotes a short paragraph to chorea (apparently the ordinary nondementing type) caused by syphilis (apparently constitutional or vascular).

Draeseke<sup>2</sup> has reported a very interesting group of cases exhibiting a combination of chorea and paresis, of the same general type as the two cases here described. In his cases there was, of course, no serologic report. He gives four cases from Ganser's Clinic, together with several cases from the earlier literature.

The serologic analysis of cases usually gives a basis for differentiation of those with syphilitic etiology much earlier than is possible on clinical grounds alone (Lowrey<sup>3</sup>). This fact, together with the many syndromes now clearly established as being at times associated with neurosyphilis (Lowrey<sup>1</sup>; Southard and Solomon), indicates the extreme importance of lumbar puncture in psychopathic patients, whether there be clinical signs or not. Our cases very clearly demonstrate this point for the organic types. They also open anew the vexed question of the etiology and pathology of the choreas of advanced adult life.

#### CASES

CASE 1.—K. B., a female of Scandinavian descent, was admitted to Danvers State Hospital June 20, 1896, at the age of twenty-eight. An adequate history was never obtained. She had had *chorea* at fourteen years of age.

For about ten days she had been excited, frightened, talkative; spoke of being

"bitten by serpents." Would let no one approach her for fear they were devils.

When admitted, she was hallucinated, hearing a child crying and seeing a woman carrying it away. She saw serpents, which she said bit her. Fingers and tongue tremulous; pulse 104; physical examination otherwise negative. A diagnosis of "acute mania" was made. (It may be noted that the hallucinations were of the scenic type, which are most common in the toxic and epileptic psychoses).

1897.—Periods when better varied with spells of violence and periods of confusion and disturbance due to vivid visual hallucinations (angels, animals, coffins).

1898.—Further attacks.

1899.—Quiet—working in laundry.

1900.—*Twitching in left arm*—irregular jerking movements. Peculiar grimaces. *Said to have had these for a long time.* Gait irregular. Speech slow and indistinct. *Demented.* Irritable.

1901.—Jerking movements worse. *Pupils unequal; no direct or consensual reaction to light.* Knee jerks very active, left greater than right.

1905.—Jerky movements have continued. Spurious ankle clonus. Pupils gray. Vision unimpaired. No pupillary reaction to light.

1906.—Temperature. Loud systolic murmur heard. Rhythm irregular. Accentuated aortic second sound. Arteriosclerosis. Albuminuria.

1907-1910.—General condition good. Continues choreatic; disoriented; amnesic.

1913.—Dysentery with recovery. Pupils stiff.

1914.—Partially oriented. Hears "water running in ears." Choreatic movements marked. Heart examination negative. *Pupils react to light and distance.*

1915.—Demented, deluded, confused.

1916.—Disoriented, memory defect, speech difficult, marked chorea. "Is a typical case of (Huntington's) chorea. The gait is extremely unsteady. Knee jerks exaggerated. There are constant coarse, involuntary movements of the hands, head, facial muscles and tongue. There is considerable dementia. The pupils react."

At this time we did blood Wassermann tests on all of the patients in the colony group where the patient was cared for. The blood Wassermann was positive, so the spinal fluid was examined. The Wassermann was positive; there was albumin and globulin excess; 3 cells; gold 444555321.

In December, 1917, the chorea was marked. There were several burns from rolling against the radiator. Demented. Speech difficult.

Summarized, we have a case with a confused, hallucinated, excited condition coming on at twenty-eight years; with onset of choreatic movements at about thirty-two years. Dementia came rather early. For several years the pupils apparently did not react—when seen by us the reaction was fairly normal. For years—at least fifteen—the clinical picture was that of a degenerative chorea. It was only by accident that the paretic serology was

discovered. Even then, careful study did not show any clear-cut symptoms of paresis.

The patient died January 8, 1918, of arteriosclerosis and bronchopneumonia. The autopsy was performed five days postmortem (C.E.S.). There were: emaciation (length 148 cm., weight 34.8 kg.), scars of burns, irregular pupils, signs of senility, enteroptosis, perimetritis, coronary and general arteriosclerosis with calcification, valvular sclerosis, chronic myocarditis, adhesive pleuritis, bronchopneumonia, hypostatic congestion, chronic nephritis, small adrenal hemorrhages.

*Head.*—Scalp thin and not adherent. Calvarium: F. 8; T. 5; O. 6. Slight generalized thickening of dura. Congestion of subpial vessels. Milkiness of pia over vertex: less marked laterally and on base, except that over the orbital surface of frontal lobes the pia is markedly thickened and gelatinous. Brain weight 1420 gm. Generalized softening of brain (postmortem).

The brain was hardened in 10 per cent formalin, and after external photography (Figs. 1 and 2) the hemispheres were divided. The appearance was very striking (see Figs. 3 and 4). The fornix was not to be discovered, and the structures involved in the wall of the third ventricle were much eroded, as were the walls of the lateral ventricles, the optic nerve and midbrain. A part of this is undoubtedly due to postmortem change. On coronal section there is rather marked internal hydrocephalus. (The erosion shows very plainly.) The brain structure is not especially altered otherwise, except for the absence of fornix, septum lucidum, etc. (Figs. 5-8.) The basal ganglia are possibly somewhat small, but not otherwise abnormal. The posterior and descending horns of the lateral ventricles are partially filled with a gelatinous, gray material which is adherent to the wall and resembles somewhat gummatous exudate. There are no other signs of gumma.

The gross brain findings are for the most part typical of paresis, although the gummy exudate and internal destruction are not.

In sections from various cortical areas (right and left frontal, precentral, postcentral, temporal and calcarine) we find parietic lesions—infiltrative meningitis, and in the cortex, perivascular infiltration, gliosis, degenerated cells, satellitosis, and capillary proliferation. Exudative cells are present in some areas where no vessels can be made out. There is, in some sections, a striking *thickening of the vessel walls*, occasionally with hyaline changes, resembling ordinary arteriosclerosis except for the perivascular infiltration. Irregularly distributed cell loss is very marked.

Sections were also taken from right and left caudate and lenticular nuclei, thalamus, red nucleus, dentate nucleus, medulla, and spinal cord.

Examination of the sections from the basal ganglia shows fairly well-marked perivascular infiltration; marked thickening of the vessel walls; accumulation of mononuclear cells in the lumen of some of the small vessels; marked cell loss; satellitosis; gliosis; in some areas large numbers of thickened vessels. In some sections, particularly in the thalamus, there is marked pigmentation of nerve cells. (Figs. 9, 10 and 11.)

Our material does not allow us to say anything regarding differential locus of lesion,—rather the lesions are very widespread, involving all of the corpus

striatum, cortex, bulb and cord. Hence it offers little of value in establishing the true pathology of degenerative chorea.

A striking point is the marked hyaline thickening of the vessel walls, resembling thus the vascular type of syphilis rather than the parietic. However, with the cell degeneration and losses, gliosis and meningitis, it seems clear that the lesions are at least of a mixed type, with more evidence in favor of paresis. In view of this, the unusually long course of the disease is of great interest and of therapeutic importance, since the benignity of the process indicates that it would respond well to treatment.

Accordingly, we may summarize the pathologic findings by saying that there was an atrophic brain, with meningitis, internal hydrocephalus, gummy exudate in the ventricle; and a microscopic picture of a rather mixed type, but with more evidence for paresis than vascular syphilis.

CASE 2.—E. S., a widow, sixty-eight, of American descent, was admitted to the Psychopathic Hospital on Jan. 21, 1918; said to be depressed with suicidal threats and periods of excitement. She had not slept well, was said to shout and cry out all the time, and wanted to be shot dead or allowed to go out and drown herself.

The history was given by a daughter. Patient's maternal grandfather died in a hospital for the insane. He is said to have been periodically insane. The attacks of mental disturbance, thought to have occurred about once a month, were very violent. The maternal grandmother was a "little queer" as she grew older. The father, a nonalcoholic stonecutter, who had deserted his family and lived with a woman to whom he was not married, died at about fifty years of age of cerebral hemorrhage. The mother died at eighty-two, of cerebral hemorrhage. One of her brothers was a "little queer." One maternal aunt was for forty years in insane hospitals, with periods of apparent recovery when she was at home. The twin sister of this aunt was queer for many years, but was not in an institution. A maternal cousin has had attacks of mental illness, thought to be similar to that of the patient. His sister is reported to have had a similar trouble.

Of the siblings, the patient is the oldest. A brother is a periodic drinker, who says the impulse comes to drink and he can't help it. Probably has had delirium tremens. Another sister died of scarlet fever.

Patient was born in 1850, grammar school education. Always a great reader; of normal habits. She always worried, was very apprehensive over trifles; not much depression; fairly social; self-willed; not much interested in the welfare of people outside of her family. She has been twice married. First husband died of appendicitis, the second husband was alcoholic. He died about sixty-four, of "paralysis of the insane," at a State Hospital where he had been about three years. The oldest son, at the age of thirty-two, had some trouble with his legs; could not walk. Recovered after treatment. Nonalcoholic; engineer. Two daughters are not in good health. One is very nervous; the other has uterine trouble.

At fourteen, the patient had typhoid fever, and is said to have been delirious. Has had more or less "rheumatism" for many years. Since the birth of her child, thirty-seven years ago, patient has been subject to diurnal (never nocturnal) incontinence of urine under excitement or physical exertion. No syncope.

About four years ago, the patient had an attack of what was supposed to be pertussis, and began to fail in health. She could not hold her artificial teeth in place; occasional "twisting of the face," unaccompanied by other symptoms, was observed. A little later she became very slovenly and unclean. It became difficult to persuade her to change her clothing after incontinence. Step-page gait at times for two years. She has been restless; constant movements of the hands; no difficulty in grasping or holding objects; no vision in one eye for a year. For about a year has talked of poverty; said her daughter did not have enough to eat. At times would go to bed "to die," saying that she could not live another minute. "I am all gone, you can see." At times she showed considerable temper. Has been worrying about her granddaughter, saying she has nothing to eat and nothing to wear. Of late has become clean about her person.

Three days before coming to the hospital, patient said she was about to die, became very excited, stamped and "hollered," got out of bed, asked why she should have a comfortable bed while the others were freezing. Two nights later, she was up all night, laughing and talking so that she disturbed the neighbors; having been quiet in the interval. She often threatened suicide, did not attempt it. Her doctor had advised that she be sent to a hospital a year ago, and with her spells of violence, this was done.

On admission, it was stated that the patient had been depressed for about six months at the time of her husband's death. Following that she became active and talkative and of late has become quite incoherent; often quite excited, striking her relatives. She called herself a "crazy old woman;" said she was too dirty to be allowed to remain here.

On examination, many coarse, choreiform movements were observed of the limbs, face, tongue and trunk. They were rather more marked in the lower than in the upper extremities, and resembled, very closely, the coarse, uncoordinated movements of Huntington's chorea. At times she was quiet and agreeable, at others cross and irritable. At times somewhat depressed. She was not very accessible to questioning, usually because of her irritability. If crossed, she would become very noisy and disagreeable, throwing herself about, but for the most part was fairly quiet. She was fairly well oriented, could give the day and date, place and persons.

No satisfactory account of her recent experiences could be obtained. She had no knowledge of current events. Was able to give the history of her early life fairly well. Her school knowledge was poorly retained.

At one time she thought she was going to die; that all about her were going to die; that she was put here so her daughters might be rid of her. Knew that her daughters were starving to death; that the children would be killed. Became excited and much agitated over this. Seemed greatly worried by the sorrows and poverty of the world. At times she was very confused in her thinking and her answers; did not realize her own condition.

Physical examination showed that she was somewhat emaciated. Skin dried and atrophied. Some ecchymosis. Diminished hearing, especially on the left. No vision in the right eye. Ptosis of the right eyelid and external strabismus. The right pupil was irregular, and *neither pupil reacted to light or accommodation*. Slight clouding of the right cornea. Absent teeth. Marked twitching of the muscles of the face and fingers. Lower jaw continuously in motion. Gait unsteady and swaying. Positive Romberg. Knee jerks active. Coordination fairly good. (In other words, general choreiform movements.) The heart was of normal size. Sounds of good quality. Pulse 88. Blood pressure 120-70. Lungs negative. Abdomen negative. The urine was negative, except for some bacteria and white cells. The Wassermann reaction, on serum, was negative—(two tests) and on the spinal fluid unsatisfactory, because of contamination. However, the spinal fluid showed globulin excess, 11 cells and a gold reading 5444433332, on the first examination; and globulin excess, albumin excess, 15 cells and a gold reading 5443333221 on a second test. Two further Wassermans on the blood serum were negative, but the Wassermann test on the spinal fluid was positive and all the other tests were similar to those already reported.

Here, then, we have a family history of cerebral hemorrhages; (probably) manic depressive psychosis and periodic drunkenness, but none of chorea. Probably of more importance is the history of paresis in the husband. The patient was apparently of good make-up—not cyclothymic. Choreatic movements and deterioration seem to have begun at the same time. At the time of our examination the case might easily have been taken for Huntington's chorea, although irritability, depressive ideas, and conduct disorder were much more marked than is usually the case—indeed the case at times seemed like a mixed manic-depressive condition. The only sign for paresis was the pupillary reactions, and it is well known that pupils that are *stiff to both light and accommodation are not diagnostically absolutely significant of paresis*.

However, the serologic evidence leaves no doubt that in this case we have to do with a case of neurosyphilis. Granting this, then the dementia and conduct disorder and choreatic movements are all to be explained on the same basis. In the light of experience, and especially in view of the active mental symptoms, we hold to the opinion that this is a case of general paresis. It is desirable to treat the patient according to modern methods and ascertain the results. The case also demonstrates clearly the fallibility of depending on a blood Wassermann alone for evidence of neurosyphilis.

## SUMMARY

Two cases are presented in detail. One, originally diagnosed acute mania, showed choreatic movements and dementia for eighteen years before death, the serology of paresis being discovered two years before death. The autopsy shows characteristic lesions of paresis plus endarteritic changes; general cell devastation and gliosis, perhaps more marked in the basal ganglia; and certain changes of an uncertain character (in part postmortem?) We can not determine the locus of lesion from our material.

The second case seems to represent a case of conjugal paresis; with chorea and dementia for about four years, with marked conduct disorder and certain depressive ideas. With the exception of the negative blood Wassermann, the serology is typical for paresis.

We believe that such cases prove the importance of performing spinal fluid tests in all psychopathic patients—certainly in all with any organic disease.

Choreatic paresis is apparently rare, judging by the small numbers of cases reported, and these are apparently the only cases in the literature in which serologic tests have established the diagnosis.

Apparently, the prognosis for duration of life is good; intensive therapy should accordingly yield good results.

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- <sup>3</sup>Lowrey, L. G.: A Study of 58 Cases Diagnosed as Paresis in Pre-Wassermann Days at Danvers State Hospital, *Jour. Nerv. and Ment. Dis.*, 1916, xliii, 324.
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## EXPLANATION OF FIGURES

Fig. 1.—Basal surface of the brain. Note the thickening of the vessels. The pontine softening does not show well. Some meningitis seen. Mag. ca. 0.7.

Fig. 2.—Vertex. Shows the moderate meningeal thickening. Mag. ca. 0.7.

Fig. 3.—Median surface of left hemisphere. Mag. ca. 0.7.

Fig. 4.—Median surface of right hemisphere. Mag. ca. 0.7.

Very striking is the absence of the fornix and septum lucidum, so that one looks directly into the lateral ventricle. The irregular, eroded surface of the



Fig. 1.

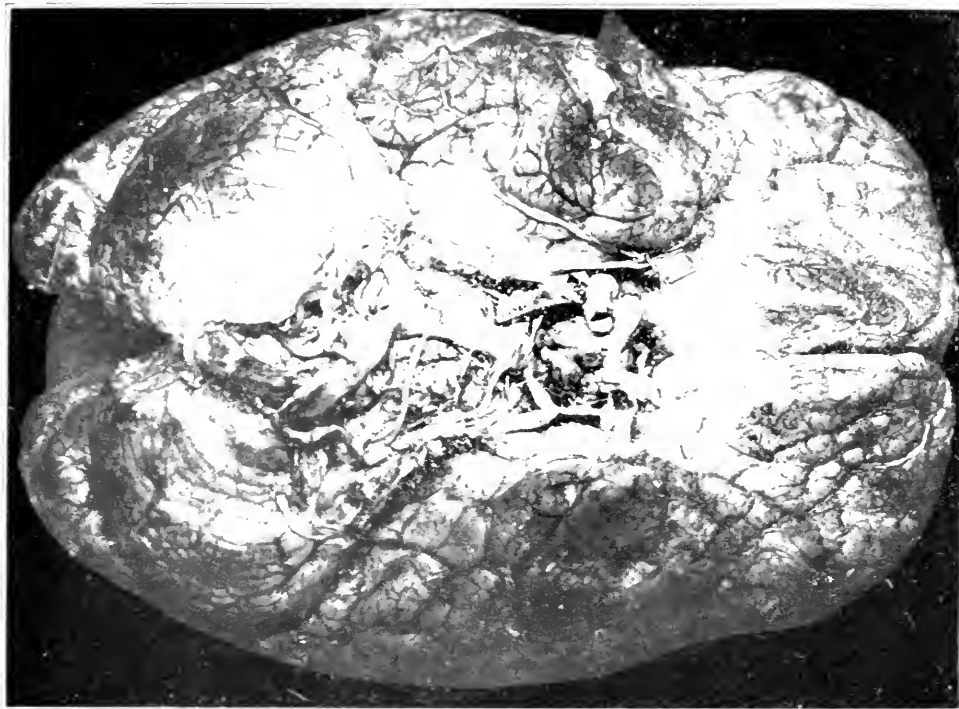


Fig. 2.

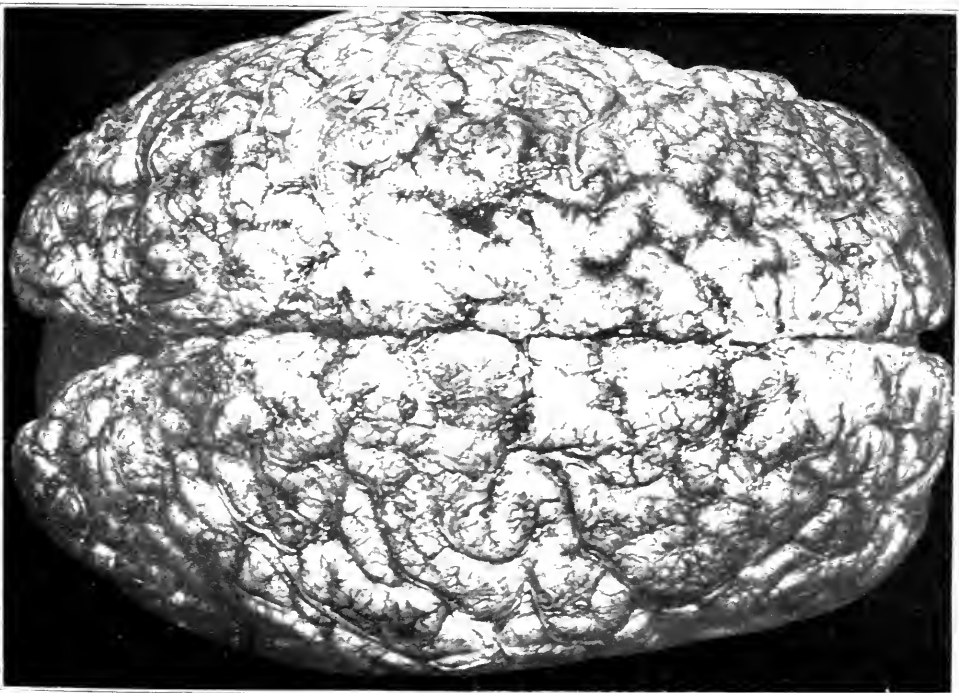






Fig. 3.

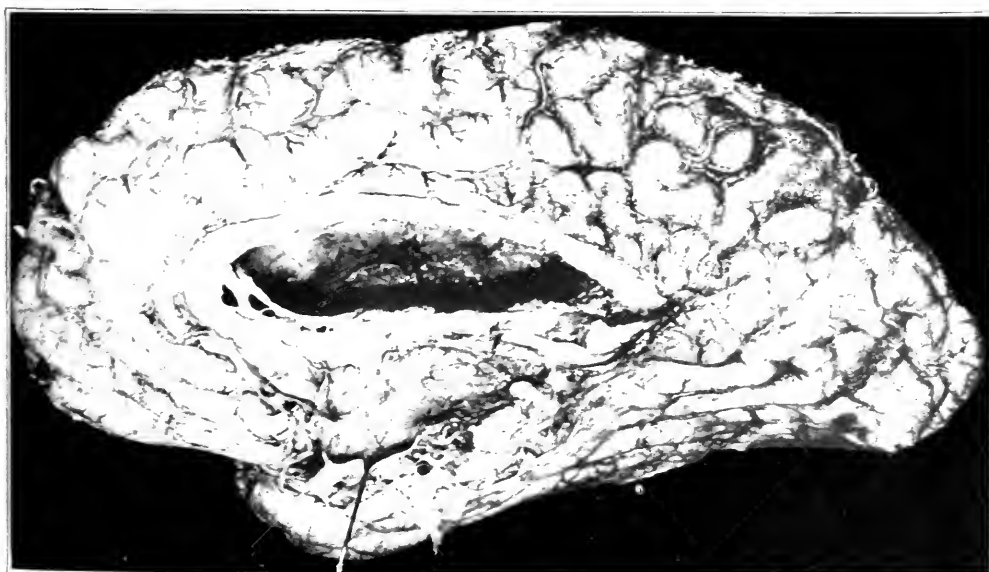
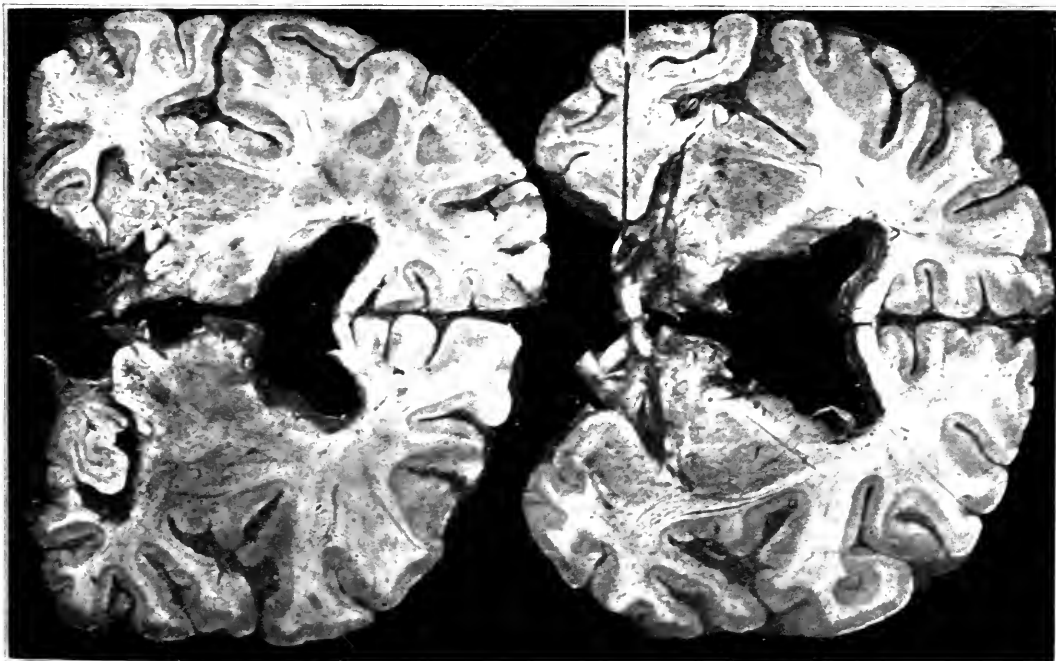
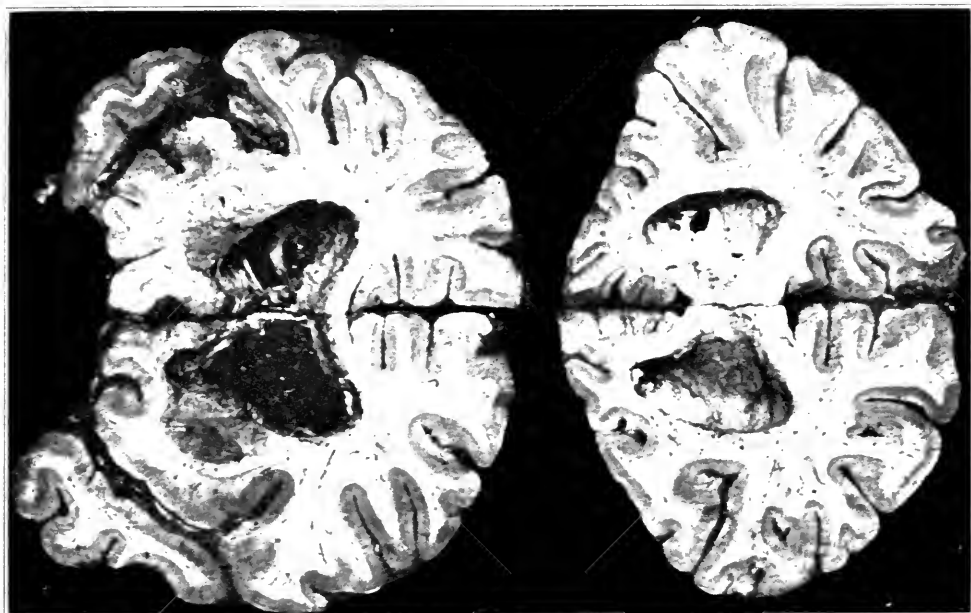
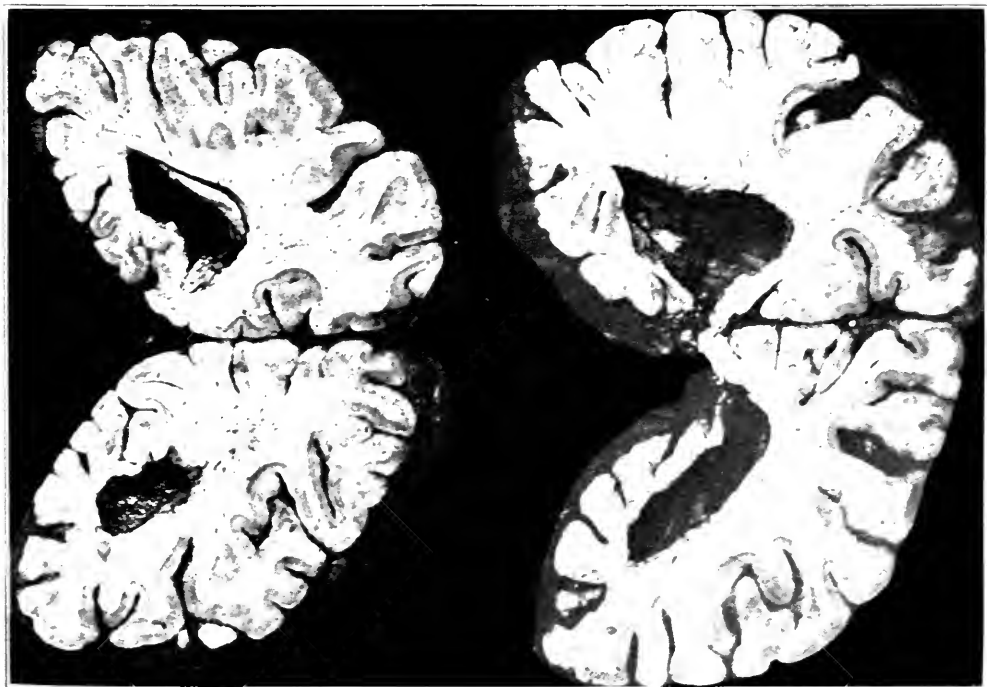
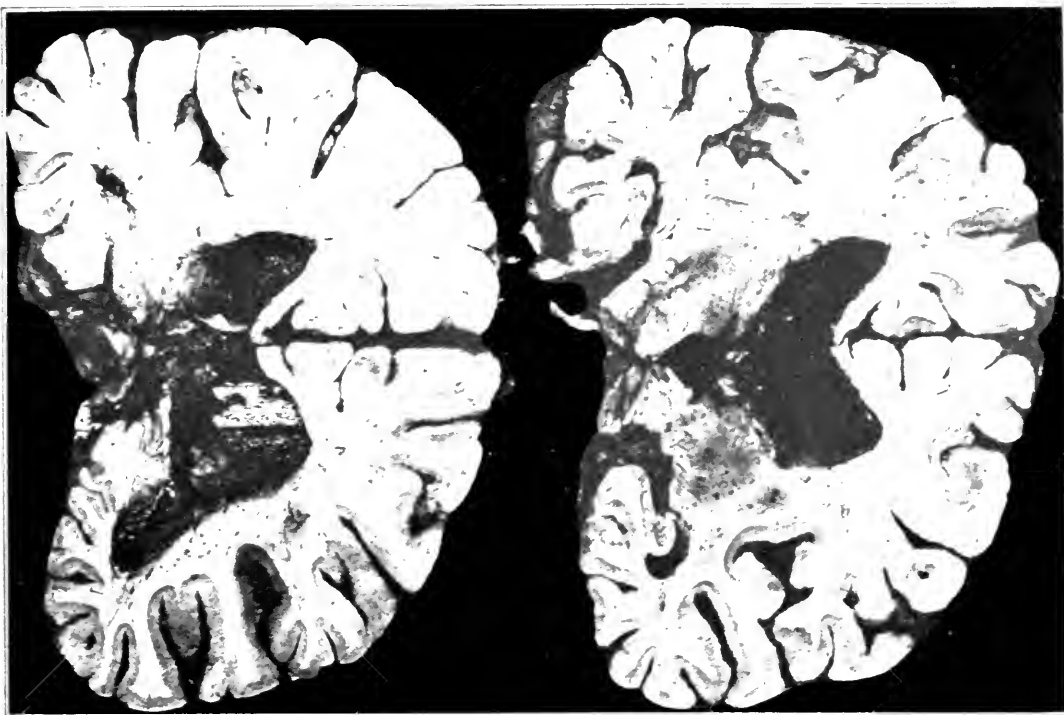


Fig. 4.













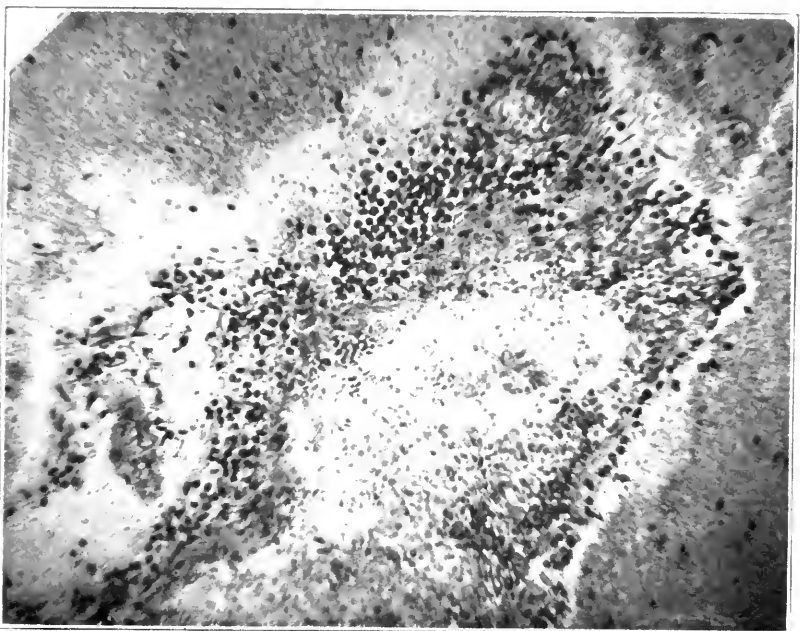


Fig. 9.

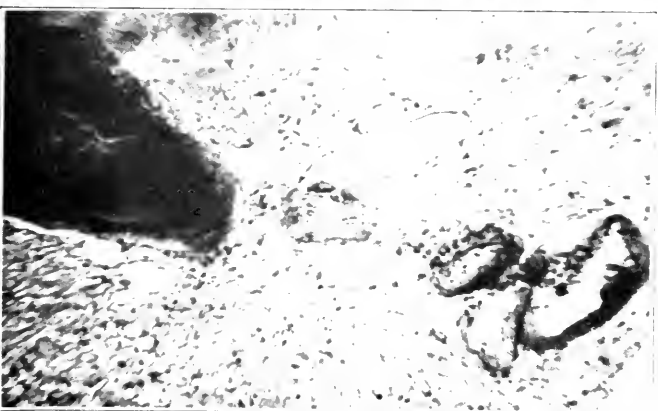


Fig. 10.

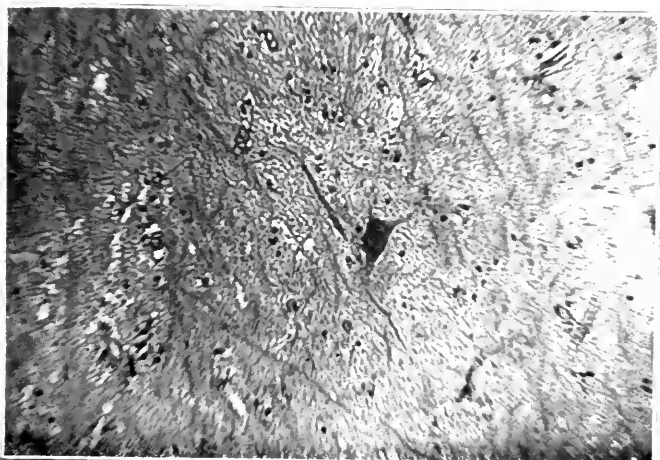


Fig. 11.



wall of the ventricles shows fairly well. The corpus callosum is somewhat thinned centrally, implying a loss of association fibers. The appearances in the temporal lobe are related to the internal hydrocephalus affecting the descending horn of the lateral ventricle. Note particularly the great thinning and erosion of the optic nerve, shown at X, Fig. 4. Mag. ca. 0.7.

Figs. 5, 6, 7, 8.—Coronal sections at interval of 1 cm. through the extent of the ventricles. Mag. ca. 0.7.

These sections show the internal hydrocephalus very well. The apparently more marked condition on the right is due to slight variation in the level of section in the two hemispheres. The basal ganglia are perhaps somewhat small and vessels are rather numerous, but there are no obvious gross lesions. The roughness of the ventricular walls is apparently in part due to postmortem changes. The absence of the median interventricular structures produces a rather striking appearance. In Fig. 6, upper section, note thinning of optic nerve at X. The cortex is apparently of normal thickness. The gray gummy exudate in the posterior horn shows in Fig. 8 in the left ventricle. No other areas of degeneration found in these sections.

Figs. 9, 10, 11.—Photomicrographs showing lesions. All sections are from the thalamus.

Fig. 9.—The mononuclear cell exudate in a perivascular space. A vessel takes up the majority of the picture. This contains red cells. In the perivascular space are the exudative cells. Mag. ca. 250.

Fig. 10.—To show the hyaline thickening in the wall of the vessels. The three vessels above show this quite well. The larger vessel below is very thick walled, but not well shown. Mag. ca. 100.

Fig. 11.—An area showing the paucity of cells and gliosis, chiefly of the fibrillary type. Mag. ca. 200.

## A REMARKABLE CASE OF OSTEOPOROSIS IN A NEGRO

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(Received for publication, June 17, 1918)

THIS CASE is a dissecting table one from Bellevue Hospital, New York City, and its full history is not known. It would seem that the head alone was secured, and eventually came to one of the anatomical establishments of Rochester, N. Y., where it was prepared for museum exhibition. A label on the specimen merely states "Colored Male; age 24," without a line describing the condition of the rest of the skeleton, with respect to any ravages the disease may have made on it, or, perchance, on the soft parts. Eventually the fact became known to me that this negro had died from tertiary syphilis, while later on the skull was purchased for the Army Medical Museum, of the Surgeon General's office at Washington, where it is now upon exhibition.

Of all the thousands of skulls and crania that I have examined, many of which have exhibited the ravages of the disease from which this negro suffered, I have never met with one that in any way equalled the amount of osseous destruction to be seen in this extraordinary specimen. In so far as my knowledge carries me, the one most nearly approaching it is to be seen in a syphilitic skull in the Pathological Museum of McGill University, and described in Volume II. of the "Principles of Pathology" by Adami and Nicholls (p. 1075, Fig. 280).<sup>1</sup>

As is well known, in syphilitic osteoporosis of the calvarium multiple gummata frequently form; and, as the disease attacks the cranial vault, the destruction of the osseous parts gives rise to complete perforation of the tables. These perforations vary in size as well as in locality and outline. In the McGill specimen they are of no great size; while in the specimen here being described they are not only numerous, but two of them at least are very extensive. The larger of these two is situated centrally in the frontoparietal

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<sup>1</sup>For further literature see Herxheimer, Lubarsch und Ostertag's *Ergebnisse*, 12, 1908.

region and is well shown in Figs. 1 and 2. It has a length of about two inches by one in breadth, with cultrate margins all around. For the most part, especially anteriorly, the disease has eaten away the external table of the skull and all the diploic tissue, and rendered the vitreous table very thin. The posterior perforation is also situated in the median line, occupying an occipitoparietal site. Smaller perforations are in evidence laterally as well as posteriorly. As will be noted in Figs. 1 and 2, the external table now only consists of an irregularly corroded surface, as though it had been acted upon by some strong acid—so powerfully in various localities as to eat its way clear through. This destruction was greatest over the entire vault of the cranium, being checked laterally, upon either side, by the squamosal suture of the temporal and the alisphenoid, and posteriorly by the lambdoid suture on the right side, while on the left side a large part of the parietal, posteriorly, was not involved.

On the facial aspect of this skull the ravages of the disease were something fearful, and the bony parts are largely destroyed over various areas. For example, the roof of the mouth, including the alveolar process upon either hand, is almost entirely eaten away, exposing the roots of the molars. More posteriorly the pterygoids are to some extent involved, and especially the body of the sphenoid.

Posterior to the foramen magnum, the occipital bone seems to have almost entirely escaped general destruction, and this seems likewise to be the case with the basilar parts of the temporal bones, including the styloid processes, which latter are not very well developed. Within the nasal cavity complete destruction took place, even to the extent of cutting away both floor and roof: eliminating the vomer and all the turbinals, and eating into the bony wall upon either side to a large extent.

This negro's face must likewise have given every evidence of the terrible disease of which he was a victim; for the external surfaces of the superior maxillaries are much abraded by the disease, and this, to a slight extent, is the case with the corresponding surfaces of the mandible and other bones of the face, especially the lower ends of the nasals, which practically have been entirely destroyed. The inner surface of the mandible is smooth, and was not attacked by the disease.

There is a specimen of this sort in the collections of the Army Medical Museum (No. 10032, Path. Series),—it being carried as a "Syphilitic Skull." It has the following history attached: "Woman over 60 years old, died of syphilis in 1868-69. She was mentioned in Dickens' 'Notes of American Travel,' Chapter XIV, as the 'funny old lady who was an upper domestic' in the hotel at Sandusky, Ohio, in 1842." The mandible is missing, but "No. 10033 shows healed fractures of left tibia and fibula."

In this case, the disease, in so far as the skull is concerned, was confined to the calvarium where it had completely destroyed the skull over almost the entire vault, especially in the parietal region. It extended further down on the left side than on the right, while the face was apparently not attacked at all.

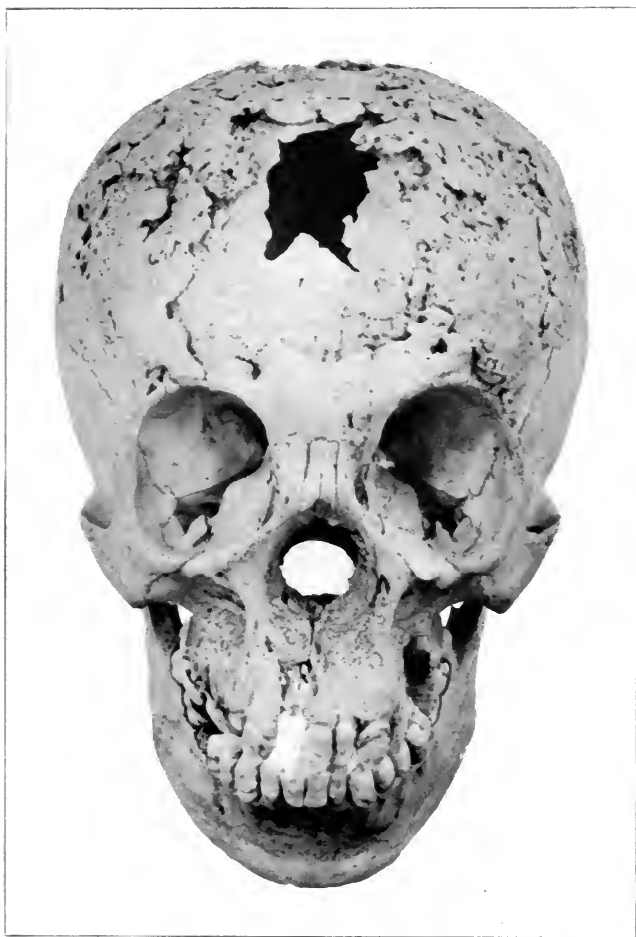


Fig. 1.—Facial aspect of skull of negro exhibiting destruction caused by syphilitic osteoporosis.  
(No. 10032, Coll. Army Med. Mus.)







Fig. 2.—Same skull as in Fig. 1, showing the cranial vault of the two perforations.





Fig. 3.—Same skull as shown in Figs. 1 and 2, seen upon right lateral view.



## SYPHILIS OF THE EPIDIDYMIS WITHOUT INVOLVEMENT OF THE TESTICLE: REPORT OF CASE

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(Received for publication, June 28, 1918)

THE recognition of a pure case of syphilis of the epididymis suggested a review of the recent literature and resulted in a surprising meagerness of articles bearing on this subject. A careful search through the Index Medicus and Catalogue of the Surgeon General revealed but one article directly bearing upon this topic since 1906.

Recourse was then had to several textbooks with the result that reference to the subject was found to be very scanty and rather unreliable. For example, Osler has practically nothing to say except in describing syphilitic orchitis, where he notes "The gummatous growth is sometimes difficult to distinguish from tuberculous disease. The area of induration is harder and it affects the body of the testes, while tubercle more commonly involves the epididymis."

Barker in his *Monographic Medicine*, otherwise so remarkably detailed does not even mention lues of the epididymis.

Keene in his *System of Surgery*, says, "Tuberculosis of the epididymis and testicle is next to gonorrheal inflammation, the most common disease of these organs, and the disease in the overwhelming majority of cases begins in the epididymis and extends later, as a rule, to the testis proper. Syphilis of the testis affects in almost all cases, the testis proper, differing sharply in this regard from tuberculosis which usually attacks the epididymis first. This fact is of much importance in making the differential diagnosis. The disease is usually limited to the testis proper."

Keyes in his book on *Syphilis*, 1908, notes that he has in one instance seen syphilis begin in the epididymis as a rounded nodule, the size of a marrow-fat pea, and to progress by the addition of other nodules in the epididymis.

Lloyd Thompson in his recent book on *Syphilis*, 1916, says on page 282, "Syphilis of the testicle occurs in two forms, as a diffuse orchitis or epididymitis, or gummata. In either case the process usually begins in the testicle and later involves the epididymis. The epididymis may or may not be involved. If it is involved, it is usually secondary. Tuberculosis is more frequently found in the epididymis."

Sir Jonathan Hutchinson in his work on *Syphilis*, 1913, says on page 207, "Many observers have noted, in the secondary stage, slight enlargements of the head of the epididymis rapidly disappear under treatment. As a rule the vas and the epididymis escape implication; but there are exceptions, and we can by no means rely upon the position of the deposit as a means of diagnosis. There are certain rare cases in which the vas and the epididymis alone suffer." He mentions a case in which a man seven years after the primary lesion had some leucoplakia of the tongue which quickly responded to iodide of mercury. Six months after leaving off the treatment for his tongue, he came with a lump as big as a hazelnut in one epididymis. It felt as much like tubercle as gumma, but it vanished so quickly under specific treatment that there could be no doubt as to its real nature.

The single reference in the literature since 1906, which directly refers to syphilis of the epididymis, is the following: Iacobovici, I. Un cu de epididimita sifilitica, Spitalul, Bucuresci, 1912—32:360. Unfortunately this article was not accessible.

Accordingly in the past twelve years, there has been practically no reference to this condition and a perusal of a few of the more generally used textbooks revealed but very cursory mention, and that rather inaccurate.

Apparently the most complete article of fairly recent date that has appeared upon this subject, is that of Micheel, which appeared as an Inaugural Dissertation in 1906, and the following brief historical notes were obtained from this excellent monograph.

#### HISTORICAL

There are references to syphilitic disease of the testicle in the writings of the sixteenth century, but at that time all diseases of the genital organs were lumped together and entirely misunderstood. In 1736, Jean Astruc first differentiated between the acute inflammatory character of gonorrheal disease and the chronic indolent form due

to lues. This was later clearly emphasized by Bell who was the first probably to point out that gonorrhea affects the epididymis primarily, whereas syphilis as he thought, confines itself strictly to the testicle. But this sweeping differentiation was later modified by Cooper in 1837, who first directed attention to occasional occurrence of syphilitic involvement of the epididymis secondary to lues of the testicle. Ricord in 1843 finally decided, after previous publication to the contrary, that the epididymis was never involved in syphilis, and backed by his great authority and prestige, this remained the belief for many years. Kocher in 1880, grouped syphilis of the testicle into two types, interstitial orchitis or syphilis of the testicle, and gumma of the testicle. He maintained that the testicle was diseased primarily and only rarely was there any spread to the epididymis. The vas deferens with the rarest exception remained free.

It was Dron in 1863, who first published instances of syphilis primarily affecting the epididymis. He reported fifteen cases of syphilis of the epididymis where there was no involvement of the testicle.

Among the French clinicians, Fournier especially, and Balme, Reclus, and Pascalis, corroborated this observation and added cases of their own.

In Germany this was not admitted even by Virchow. Pinner, however, in 1884, was the first to insist upon the accuracy of Dron's reports and added three cases of his own. Rosenthal in 1891 demonstrated an unquestioned instance of syphilis confined to the epididymis (without involving the testicle). But Lewin of Berlin, Neumann in Vienna, and Pick of Prague, all with enormous material at hand and recognized as careful observers, refused to admit a pure syphilis of the epididymis. Micheel, however, in 1906, emphatically substantiated the claim of a pure syphilis of the epididymis and contributed a case of his own.

#### COURSE OF THE DISEASE

The disease can readily be overlooked unless properly sought after, since in the majority of cases the swelling of the epididymis is entirely painless. Balme observed thirteen instances in 2300 syphilitics. Dron happened to see fourteen cases in two hundred syphilitics. Our case reported below, was drawn to our attention because the patient himself complained of the mass since it was extremely tender. The case of Micheel falls into a similar category.

Fournier observed eight cases occurring between four and five months after the chancre, six cases occurring between five and fourteen months after the primary lesion, eight cases occurring between two and eight years after, and one case fifteen years after the initial sore. Our case occurred nine years after the chancre. The majority of cases reported in the literature occurred during the secondary stage just as in the case of syphilis of the testicle. In this stage, both epididymi are usually involved consecutively while in the tertiary stage, only one side is affected as a rule. Occasionally softening of the mass with rupture of the contents and a consequent fistula occurs.

There would seem to be two clinical types, one slow and painless, the other acute and painful. In the former type, the disease develops gradually, insidiously, and without pain. Frequently it is not noticed by the patient and is overlooked by the physician. In a small percentage of cases, deep, dragging pains are felt in the scrotum and along the inguinal canal. The epididymis shows an irregular, indurated surface. Individual thickenings vary in size from a pea to a nut usually situated at the head, less often at the tail of the epididymis. The consistency is firm and hard. Pressure is only slightly painful, if at all. The testicle can always be sharply distinguished and the vas deferens can likewise be isolated. There is no change in the skin of the scrotum, and nothing abnormal is found in the prostate and vesicles. There is hardly any hindrance in walking or working.

In the acute type, the pain may be very severe, and is increased by movement or disturbance. Walking is almost impossible. The entire epididymis is involved, but especially the head. The surface is smooth and the testicle and epididymis can be accurately distinguished one from the other. After a few days the acute process subsides and there follows a chronic course as above. The testicle is not involved.

#### DIFFERENTIAL DIAGNOSIS

One must be able to exclude gonorrhea, tuberculosis and carcinoma, all of which more frequently involve the epididymis than does lues. The distinction from gonorrhea is simple. The process is more acute and there is also evidence of gonorrheal urethritis with the presence of gonococci. Carcinoma should not give much difficulty. There will be more emaciation and probably regional lymph node involvement,



which as is known, does not occur so frequently in lues. The differentiation from tuberculosis offers more difficulty and there one must depend on evidence of either tuberculosis or syphilis elsewhere in the body, upon the Wassermann test, and complement-fixation test for tuberculosis, and perhaps most of all, upon the therapeutic result.

#### TREATMENT

The treatment is purely that of routine syphilitic therapy and needs no further comment.

#### REPORT OF CASE

Patient, W. S. O. P. D. No. 18140, cook, Scotch, forty-seven years old. Came to the University of California Clinic in October, 1915.

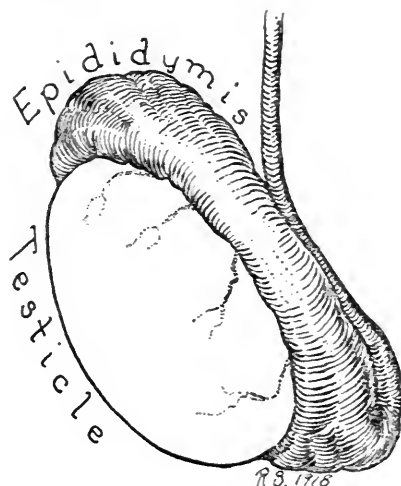


Fig. 1.—Before treatment. Testicle negative. Epididymis is enlarged and both globus major and minor hard, rounded, and nodular. Body is thickened and indurated but not nodular and nodulation at either end gradually passed into body without definite demarcation.

*Summary of Case.*—Gonorrhea six years before, treated with injections and cured within a month.

Chancre in 1906 followed by sore throat, no rash; treated with pills for one year, none since.

Now complains of painful and swollen testicle, beginning about ten months ago. Says swelling occurred on right side which disappeared in four months, and then appeared in the left side. Has lost nine to eleven pounds in the last ten months.

He came to the Genitourinary Department and there it was found that his prostate was negative on palpation, prostatic secretion clear, and the vesicles not palpable. Urine showed no shreds.

*Local Examination.*—(Dr. Hinman) (Fig. 1) October, 1915. "The left epi-

didymis is enlarged throughout, hard and elastic but not particularly nodular. The vas is thickened but not nodular. The testicle is in contrast small, however, possibly slightly enlarged."

Patient was then referred to the Medical Clinic for general examination and it was then found (Dr. Lisser) that he had unequal, irregular pupils, right larger than the left, and the left pupil barely reacting to light. He was anemic and undernourished and weighed 104 pounds. Physical examination otherwise was negative. Wassermann, positive +++ . Spinal fluid—51 cells, Nonne +, Noguchi +, Wassermann, positive +++.

*Treatment* was begun October 16, 1915. He received mercury salicylate injections, potassium iodide by mouth, and old salvarsan. After one mercury injection and .3 salvarsan, it was noted, October 22, that the scrotal contents were con-

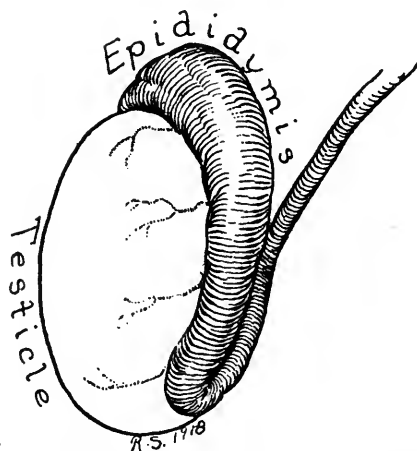


Fig. 2.—After treatment. Testicle and epididymis practically negative on palpation. Slight thickening of globus major.

siderably decreased in size and that the tenderness on the left side of the scrotum had entirely disappeared and that the right side was much less tender.

By December 31, 1915, he had received .3 old salvarsan, 9 mercury salicylate injections and considerable potassium iodide. His weight had increased eight pounds, felt much improved generally, stronger, and appetite had increased. December 31, Dr. Hinman made the following note: "The tumor of the left side of the scrotum has practically disappeared, no marked tenderness on palpation, epididymis is small, the globus major being still somewhat thickened; otherwise it is elastic throughout. The vas is somewhat thickened but not nearly so much as when seen in October. The testicle is smooth, elastic, and quite normal." (Fig. 2.)

This is a striking instance of luetic epididymitis and vasitis without much if any involvement of the testicle to be made out on palpation.

## SUBSEQUENT COURSE

Patient continued with treatment for a time and it was noted that his Achilles and patellar jerks became unequal. He remained away from May, 1916, to November, 1917, when he returned because of headaches and some failure of vision. He then had unequal, irregular Argyll Robertson pupils, Achilles jerks absent on the left and barely obtainable on the right, some paresthesia on the calves of the legs and hypalgesia in the inner side of the arms. Wassermann blood serum, positive +++, cholesterin, negative acetone. Spinal fluid—36 cells, Nonne and Noguchi strongly positive, Wassermann, positive ++.

In February, 1918, Dr. Hinman was able to examine the scrotum again and made the following note: "There is no enlargement of either epididymis, vas, or testicle. Contents of serotal sac feel negative."

## CONCLUSIONS

1. Unquestionably a condition exists in which the epididymis is affected by syphilis without involvement of the testicle.

2. Apparently this condition is quite uncommon, though probably it is often unrecognized.

3. There is a widespread misconception prevailing: namely, that syphilis only attacks the epididymis secondary to syphilis of the testicle.

4. A case is recorded which is an excellent illustration of a pure syphilis of the epididymis, without involvement of the testicle.

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## SYPHILIS OF THE STOMACH—RADIOGRAMS OF A CASE

BY SINCLAIR TOUSEY, A.M., M.D., NEW YORK CITY

(Received for publication, March 28, 1918)

THE probability of the lesion being syphilitic should be borne in mind when we find a radiograph showing very marked pyloric obstruction in a patient without cancerous cachexia. He may very likely be suffering from malnutrition and from gastric symptoms attributable to prolonged retention in the stomach. But there is a history of specific disease and an absence of the characteristic findings of cancer in the aspirated gastric contents. Considering the apparently complete obstruction, the patient's general appearance is remarkably good. Radiographically, the appearance is apt to be that of a simple pyloric obstruction with sac-like dilatation and atony of the stomach. And while there are some cases of cancer which present this sac-like appearance, they are rare and usually at a terminal stage with an unmistakable general cachexia. Radiograms of cancer commonly show a clearly defined contour of the stomach closely embracing the gastric contents whether immediately after the barium meal or six hours later. And characteristic filling defects are often seen.

The question of treatment is important. When we see every reason to think the trouble syphilitic, we can inaugurate antisymphilitic treatment and supplement the gastric feeding by high nutritive enemata provided the patient's weight and strength can be maintained in this way pending gradual improvement in the local condition and the return of sufficient patency at the pylorus. Of course a gastroenterostomy should be done before the patient becomes too weak if it becomes evident that he is failing.

The patient, Mr. K., aged thirty-six, and weighing 165 pounds was referred to the author by Dr. Robert Coleman Kemp. There was a history of syphilis beginning ten months previously and treated by mercurial inunctions. Four months ago pain in the stomach developed; and for the last month the pain had been very acute going through to the back and he had vomited about once in two days. The bowels which had always been regular had become very constipated. An hour after a test breakfast there was a residuum of 310 c.c., containing spinach taken



Fig. 1. Syphilis of stomach. Prone. Immediately after barium meal.

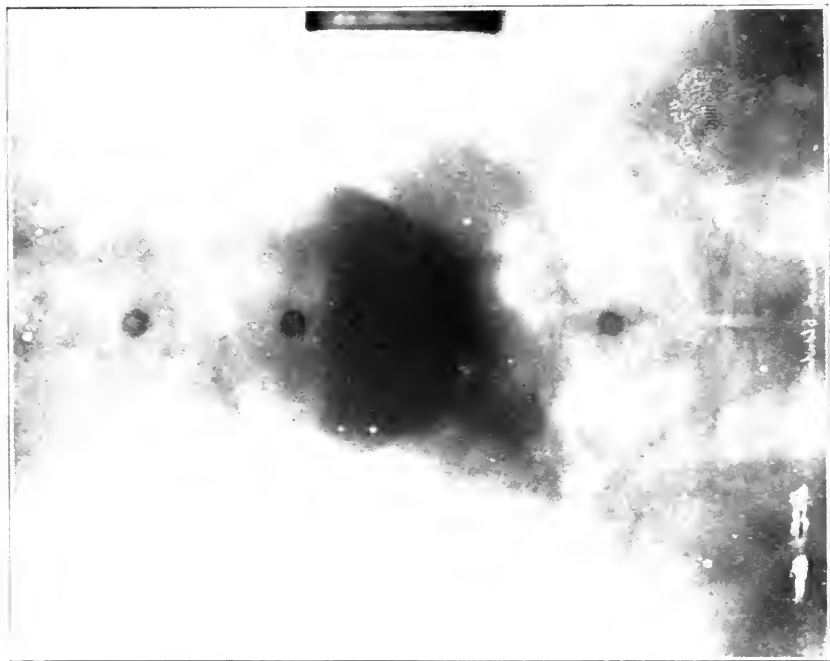


Fig. 2. Syphilis of stomach. Standing. Immediately after barium meal.





Fig. 3. Syphilis of stomach. Standing. Six hours after barium meal and directly after barium enema.

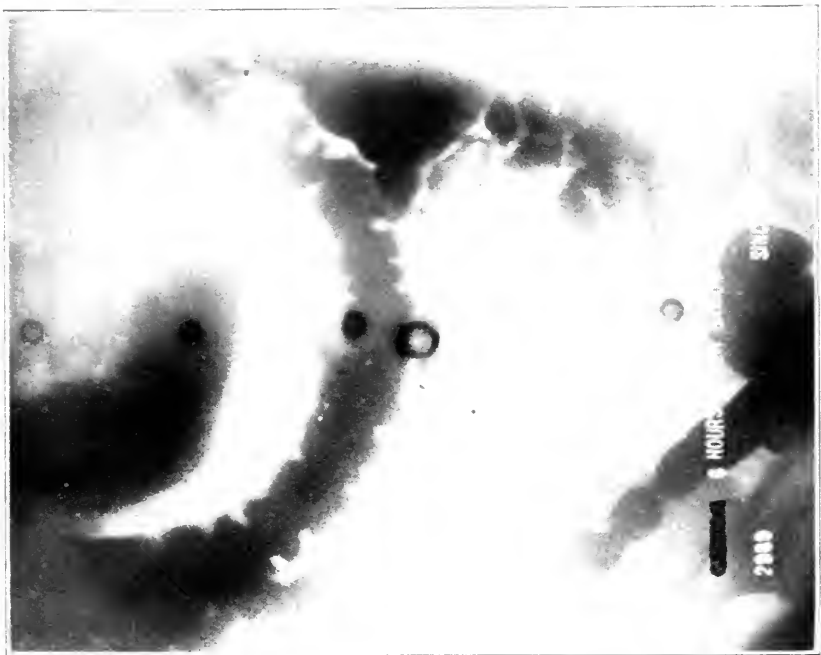


Fig. 4. Syphilis of stomach. Tousey's position (prone with pelvis 45° higher than chest). Six hours after barium meal and directly after barium enema.





at dinner the night before. No other pathognomonic change in the gastric contents.

A radiogram taken prone immediately after the barium meal showed the stomach as a shapeless mass without any filling of the duodenal cap.

Another standing immediately after the barium meal showed just a sort of pool of liquid at the most dependent part of a dilated relaxed and shapeless sac.

A radiogram standing six hours later, not reproduced here, was a duplicate of the one taken immediately after the meal. The stomach should at that time have been entirely empty and the meal should have been distributed through the last part of the small and various portions of the large intestine.

After an enema had been administered, a standing radiogram showed the stomach contents as a shapeless puddle while the large intestine was distended normally though showing some prolapse of the transverse colon. Prolonged distention of the stomach with solids and liquids would naturally produce ptosis of the transverse colon.

A final radiogram was made in the author's position, prone with the pelvis 45° higher than the thorax. This allows the colon to gravitate toward the thorax provided that it is free from adhesions, but these are shown to be present in this case. When the stomach is full as in this case the shape of the opaque meal is quite different from what it is in the erect posture.

## MENTAL DISTURBANCES AND SYPHILIS

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(Received for publication, May 9, 1918)

THE occurrence of mental disturbances is an incident in the development of neurosyphilis. Not very long ago in studying mental cases enormous stress was put upon psychological reactions, character of delusions, type of hallucinations, varieties of illusions and numerous other mental data. At present in dealing with any sort of mental disturbance, the first and most important task is the search for evidences of neurosyphilis. For practical purposes, we may classify insanity by establishing two primary groups: The group caused by syphilis and the group not caused by syphilis. The nonsyphilitic group may be dealt with in any way most agreeable for classification purposes. The choice is a wide one. The syphilitic group is the one which now engages our attention.

Southard speaks of psychopathic material as "a concentrated essence of the most difficult problems of general practice." These problems are greatly simplified by the proved fact that syphilis may be the causative factor in practically any variety of mental disturbance. The character of the mental symptoms does not furnish the essential clue which is the therapeutic clue. To say that this case is dementia precox, and that case is mania may satisfy the desire for attaching a name to each symptom group, but this is of little benefit to the patient. The first and most important thing to do is to determine the presence or absence of syphilis. How best can we determine in mental cases whether syphilis lurks in the nervous system? The determination is comparatively simple:

### 1. Clinical evidences of neurosyphilis:

Such evidences are practically limited to suggestive occurrences in the past or family history of the patient, eye symptoms, and anomalies of deep reflexes. Of these the eye furnishes the most suggestive information. Pupils irregular in contour, of unequal size, or which

react poorly or not at all to light or accommodation proclaim aloud the possibility of syphilis. Ptosis and transitory deplopia are suspicious. However it must be borne in mind that all clinical evidences may be lacking.

## 2. Laboratory examination:

The blood Wassermann should be made, the spinal fluid Wassermann, cell count of spinal fluid and globulin estimation of spinal fluid should be obtained. It must be remembered that a negative Wassermann in the blood by no means excludes syphilis. The spinal fluid may give the only clue. Thus, a man of thirty-eight was brought to me from a North Georgia town in the early winter. His symptoms were entirely mental and consisted in periods of noisy and irrelevant behavior, insomnia and confusion of thought. The clinical examination was entirely negative and the Wassermann on the blood was negative. Attempts at lumbar puncture were at first frustrated by the patient's lack of cooperation, so that it was two weeks before the spinal fluid was obtained. During these two weeks he was completely disoriented, at times noisy and restless, and at other times mute. At all times he was inaccessible. When finally the spinal fluid was obtained, examination of it revealed a four-plus positive Wassermann, 170 cells per cubic millimeter and a large increase in globulin. This patient's improvement dated from the first intravenous administration of diarsenol. He has been clinically well and at work now for several months, although his spinal fluid has not entirely cleared. The striking feature was the negative clinical examination, and the negative blood examination in a case of undoubted neurosyphilis affecting the brain.

In further proof of the contention that a deciding factor in the classification of mental cases is the determination of the existence of syphilis, I am able to produce records of idiocy, imbecility, mania, melancholia, dementia precox, paranoia, many cases of so-called neurasthenia and cases presenting a medley of mental symptoms, all of which cases have as their etiologic basis, syphilis.

A further question which now arises is how shall the various types of neurosyphilis be classified? Out of a confused mass of detail three principles stand out.

1. The most satisfactory classification is based on anatomic pathology and leads to the recognition of three types—meningeal neuro-

syphilis, vascular neurosyphilis, parenchymatous neurosyphilis, and secondarily, the combinations and permutations of these three. Thus, we would recognize paresis in the vascularparenchymatous group, since the lesions occur especially, though not exclusively, in the blood vessels and in the parenchyma of the brain.

2. The lesions are of two main varieties from a pathologic standpoint:

Inflammatory or exudative, and degenerative. A third "toxic" variety is possible. The exudative variety responds to treatment in a gratifying manner, the degenerative does not. These two varieties may and often do coexist, in which cases improvement is variable.

3. Mental symptoms or neurologic symptoms depend upon the type of lesion (meningeal, vascular, parenchymatous or their combinations), the variety (exudative or degenerative) and the anatomic location in the brain or cord:

In view of the above statement, certain questions regarding general paresis are pertinent.

Our old definitions of paresis were poorly considered. Osler, for example, defines it as "a chronic progressive disease of the brain and meninges associated with psychic and motor disturbances, finally leading to dementia and paralysis." In view of this definition, if the disease did not progress or terminate in dementia or paralysis, it was not paresis. The truth is, we can not make this disease conform to such restrictions. With many others, I feel confident that no one can successfully differentiate paretic and non-paretic forms of neurosyphilis—no matter what the psychic and mental symptoms or laboratory findings may be. The question of whether paresis is curable or not resolves itself into the question of what is meant by the term "paresis." If it is defined as essentially an incurable disease of the brain, certainly it is incurable. If it is the type or form of neurosyphilis which is destined to terminate the patient's career, willy nilly, certainly it is incurable. Why give any treatment? Kismet! It is fate! Make the patient comfortable and pray for the end. But what medical Nestor, what diagnostic prodigy, is going to make the differentiation between the form which is to be paresis and that which is not to be paresis? Why not, tacitly at least, disregard the old name paresis and recognize

only cerebral syphilis? From such a disease some recover, some enjoy remissions, while others in the face of all treatment pursue a downward path. In spite of fatalities we treat other diseases, why not thus treat cerebral syphilis whether paresis is anticipated or not?

I have now arrived at the object of this paper: Namely, to deprecate the attitude of hopelessness in the treatment of paresis, and to urge that all these cases of cerebral syphilis be treated intensively and persistently in spite of failures and discouragements. No medical progress has ever been made by adopting an attitude of therapeutic pessimism.

Paresis is not a rare disease. It is estimated that in New York state approximately 1,000 persons die of it every year—almost as many as die of typhoid fever in a year. Are we to attempt no therapy, make no effort? I wish to emphasize the fact that it is worth while to institute vigorous, and prolonged intensive treatment in these cases. Cases are constantly being reported which conform to the parietic type in all their symptoms and signs, and which recover for a longer or shorter period under such intensive treatment. The question of remissions in untreated cases is readily disposed of by the interesting and valuable observation of Southard. Says he: "We should strongly object to any account of parietic neurosyphilis which should insist that its necessary outcome is fatality within a term of years \* \* \* If nature can stop a parietic process, why can not man do as much? Can it be alleged that our own apparent therapeutic successes and those of others are merely curious examples of coincidences, namely, that remissions have chosen to occur precisely when therapy was systematically applied? The percentage of therapeutic successes with modern intensive treatment, wherever it may ultimately stand, is already too high for this hypothesis of fortuitous remissions." In proof of this statement Southard quotes 300 untreated cases of paresis which he reviewed and could find but five self-supporting and ten more in normal-looking remissions,—while in 200 treated cases, 50 were capable of self-support. I myself have under observation a case presenting the typical symptoms and signs of paresis, who after intensive treatment has been at work for more than nine months and has recently been promoted.

I feel that the hopeless attitude adopted by many asylum physicians is partly due to the fact that a large proportion of their cases arrive late, when degenerative changes of such magnitude have occurred as to preclude improvement. Even here, however, there are cases in which the symptoms result from exudative, rather than degenerative changes in the brain, and which intensive treatment might improve.

Intensive treatment does not include those half-hearted rare injections of salvarsan or its substitutes with, perhaps, mercury pills and potassium iodide. By intensive treatment is meant intravenous salvarsan or reliable salvarsan substitutes, once to twice a week over a long period. It should be given until there is improvement, or until 20, 30 or 40 doses have been administered. One of Southard's cases received 60 doses and recovered sufficiently to return to work for six months at the time the report was made. Some cases are also benefited by intraspinal therapy, and some by the associated use of mercury and potassium iodide.

#### CONCLUSIONS

1. Syphilis may cause practically any type of mental disturbance. The old idea that a case of paresis must possess delusions of grandeur can no longer be entertained. Clinical symptoms and laboratory findings are the best tests to be applied in almost all cases of mental disorder.

2. In mental cases with evidences of syphilitic infections, probably all of them become impaired as the result of syphilis. There may be contributing other causes, but syphilis is the efficient cause.

3. Having established syphilis as the cause of a given case of mental disturbance, a gross injustice is perpetrated upon the patient and his family by consigning him to parietic hopelessness. Rather, he should be thought of as a case of cerebral syphilis, who may be benefited by intensive treatment and such treatment should be persistently continued as long as there is any possibility of improvement. Some patients have apparently recovered after many months of such constant efforts in their behalf.

## VITILIGO SYPHILITICA

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(Received for publication, June 17, 1918)

IN considering acquired vitiligo, due to syphilis, and its differentiation from other pigmentary atrophies and hypertrophies we are at once struck, in studying the literature, by the vagueness and ambiguousness of the terms used. Albinism, leucoderma, vitiligo, vitiligo syphilitica, pigmentary syphiloderm, achromasia, each author seems to have a different meaning for each term. However, there is a general tendency to follow along the lines suggested by Ormsby. He divides the congenital cases into two classes: where the whole skin area is involved he calls it albinism; where only small patches leucoderma. The acquired dyschromasias he calls vitiligo, then differentiates nonluetie cases from luetic by applying to the latter the name vitiligo acquisita syphilitica.

In this paper we wish to consider these pigment atrophies from the syphilitic standpoint. How many of them are due to specific infection? In how many cases of specific affection may we expect to find white patches or spots? In such a study the differentiation into congenital and acquired types would not be as important as differentiation into luetic and nonluetic. Following Ormsby's classification we might divide the cases into leucoderma nonsyphilitica and leucoderma syphilitica, where congenital, and vitiligo nonsyphilitica and vitiligo syphilitica, where acquired. Afterward, as further causes for nonspecific vitiligo were discovered a fuller and more accurate nomenclature would require only the etiologic term after vitiligo, as vitiligo syphilitica, vitiligo tuberculosa, etc.

Pigmentation of the skin is mostly due to the presence of pigment granules between the deeper layers of the epithelial cells of the rete or prickle-cell layer. These granules are almost certainly not derived from hemoglobin, but are probably formed by the nuclei of the epithelial cells from colorless substances. After they have been formed, wandering connective tissue cells, by protruding ameboid processes between the basal layer cells, pick up these

granules and carry them deeper into the corium. This pigment is melanin and so far as we have been able to determine the pigment in the conditions under discussion is still the same melanin; the only difference discovered is in the amount of the pigment.

The universal congenital lack of pigment known as albinism need not be considered here, but a study of partial congenital pigment atrophy or leucoderma may give us some light. Leucodermic spots are present at birth, yet these spots continue to grow larger after birth in many cases, and even new spots may appear near, but unconnected with, the old ones. It is quite common for these white spots or patches to be surrounded by normal skin, instead of a pigmented border. There seems to be no other pathology than the decrease in number of pigment granules; the skin is normal to the touch, not elevated or depressed, and there are no symptoms of itching, burning or paresthesia.

Vitiligo, used in the sense of acquired pigment atrophy, may be divided for the sake of convenience into two classes. The first class includes cases not luetic or not supposed to be due to lues; the second class is considered syphilitic beyond doubt. The first class, ordinary vitiligo, is of unknown etiology, although it has been said to follow scarlatina, lichen planus, scleroderma, the menopause, nervous exhaustion, malaria, myxedema, Grave's disease, asthma and typhoid. It is also said to begin at times where there has been trauma of the skin. The use of rather strong solutions of formaldehyde upon the skin of negroes is quite apt to cause a local bleaching which may spread quite widely. There is also a pigmentary atrophy due to leprosy which may be of similar character to the syphilitic vitiligo.

Ordinary vitiligo nearly always begins as a hyperpigmentation, occurring in small spots and growing peripherally, the center becoming depigmented and the new border hyperpigmented, so that an early appearance is of one or more white spots with deeply browned margins. The entire center does not always become depigmented; cases have been reported where a small patch of pigment persisted in the center of each spot where the lesion originally began, although there might be a wide band of white around this pigmented center, between it and the pigmented border. It is usual for the white spots to coalesce in their growth, thus making a



patch of varying size and shape, but always with crescentic outlines. Sometimes several such patches coalesce, forming a large white area in which one can see some remaining hyperpigmented borders, giving the effect of a brown discoloration on a white skin. On the other hand, there are cases which begin as a brown hyperpigmentation spreading rapidly over the neck, hands and arms, but failing, however, to affect various sized islands of normal skin, which then appear to be white patches in a normal or slightly sunburned skin.

The study of the sections of the skin in this disease has as yet given us but little positive information. There is an absence of pigment in the rete where the white patch is, with some increase in the number of the connective-tissue pigment bearers, the chromatophores. At the margin of the white patch or spot, where the skin appears to be more highly colored than normal we find a decidedly increased number of granules in the rete, but no increase in the corium of the wandering cells which carry this pigment away. Leloir, in 1881, claimed to have found a degeneration of the deeper lying nerve fibers in association with vitiligo; he says that there is a parenchymatous neuritis, in which the axis cylinder degenerates and is absorbed, the myelin sheath breaks down and only the primitive sheath is left with proliferated nuclei. Many others lean toward the opinion that the condition of the skin is due to the action of the nervous system, directly or indirectly. For instance, Stelwagon says that it is undoubtedly a neurosis; others speak of a neurosis due to autointoxication. Malnutrition of the cells, change in the internal secretions, reaction to obscure inflammatory reaction, these have been suggested, but without any definite proof.

The other type of vitiligo, the pigmentary syphiloderm, has many points to differentiate it from typical ordinary vitiligo, yet at first there were few who observed the relationship of this dermatosis to lues. From 1853, when Hardy described it, until 1873, when Fournier called attention to it, we find practically nothing on the subject. In 1889 Tenneson reported a case quite interesting, owing to the location of the patches; this was a syphilitic patient who developed vitiligo on scalp, abdomen and lower extremities following an attack of alopecia. Further cases were reported by Ducassel in 1892, Pierre Mari and Crouzon in 1902, Leloir, Chabrier,

Gaucher and Pautier in 1904 and Thibierge in 1905; in each case the author attributed the dermatosis to syphilis. Gros Pierre wrote a thesis in 1905, claiming for syphilis, even in the early stages, the power of causing vitiligo.

It is quite characteristic of the pigmentary syphiloderm that it nearly always appears only on the neck, but one out of thirty cases observed by Fournier having the patches elsewhere. However, cases have been reported where the affection occurred on other parts of the body. It has a marked predilection for young brunette women. It may appear at any time during the secondary stage, although usually toward the end of the first year. It is not nearly as well defined as the other type of vitiligo and is said to have a greater tendency to symmetricalism.

From our observation we should say that vitiligo acquisita syphilitica tends to take one of two forms, either a hyperpigmentary form or a depigmented one. The first is characterized by the appearance of light brown to coffee-colored spots on the normal skin, which appears by contrast much whiter than it really is. These spots may, and usually do coalesce, leaving white islands of normal skin between the patches of brown skin. The second type also begins as a hyperpigmentation, a diffuse brown discoloration spreading over a considerable area, followed in a short time by absorption of pigment in small spots throughout this area; these spots are really whiter than the normal skin and appear still whiter by contrast with the brown hyperpigmentation surrounding them.

In either case the spots may last for months or years. There are no subjective symptoms. The patches are usually smaller than occurs in ordinary vitiligo; the spots, themselves, are seldom larger than a penny, often much smaller; they show the same tendency to coalesce into patches on the neck, where closely crowded, but when present on the trunk or flanks the spots are much more apt to remain discrete. It has been almost universally granted that vitiligo syphilitica is very resistant to antiluetic treatment, only Kaposi offering a dissenting opinion. The latter speaks of the astonishing rapidity of results from specific therapy.

The most plausible explanation of the changes which occur is to suppose that the mild diffuse inflammatory reaction which occurs where there is a moderate infection of the skin by spirochetes is

capable of causing increase in the activity of the epithelial pigment cells, with hyperpigmentation, but that when the resorptive and reparative processes begin there is an absorption of this pigment from the exhausted cells by the connective tissue chromatophores, who carry away the granules leaving almost no pigment in the rete, while the chromatophores themselves lose the pigment owing to an affinity of the spirochetes for melanin or an ability to destroy it.

Our statistics on vitiligo show that in a total of thirty-six cases, ten cases occurred in syphilitics in such a way as to suggest the probability of the lues being the cause, eight cases occurred in hereditary syphilitics, twelve in tubercular families, four in a nervous family, two in diabetics. It was not unusual to note concomitant nervous symptoms, such as headache, vertigo, insomnia, reflex changes and neurasthenia, sometimes even going on to tabes or paralysis. Cases of inherited or acquired vitiligo in the offspring of those who have had syphilis with such nervous manifestations as tabes, meningitis, epilepsy, psychoses, etc., usually give a negative blood-Wassermann. We have noted one case and Zelenev reports two similar ones, where the vitiligo manifested itself very late, 20 to 30 years after infection; what was probably a syphilitic infection of the lungs also occurred in these cases with the dermatosis. An interesting point is the observation which has been made that individuals with vitiligo have been known to become infected with syphilis.

At present our knowledge is insufficient to base definite conclusions on. That syphilis is the cause of the pigmentary syphiloderm of the neck seems almost certain; that it is the cause of certain other cases of vitiligo is probable, but it is very improbable that syphilis is the cause of all cases of vitiligo.

## ANTENATAL SYPHILIS\*

### SUGGESTED ACTION OF THE CHORIONIC FERMENTS

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SYPHILIS is perhaps the most important and probably the most frequent cause of abortions and premature deaths. The recognition of syphilis in the stillborn fetus, in the gravid mother, or the newborn child, is now much easier to establish than it was twelve years ago. The discovery of the *Spirochete pallida* by Schaudinn and Hoffmann in 1905, the means of diagnosing by testing the blood for Wassermann's reaction in 1906, rapidly succeeded each other.

I quote Dr. F. W. Mott's words<sup>1</sup> as regards the next great advance in the pathology and treatment of syphilis.

This was "the discovery in 1909 by Ehrlich and Hata of a chemotropic substance for spirochete and yet not organotropic—that is to say, a substance whereby the spirochete of syphilis could be killed without injuring the tissues. By chemotropic I mean a substance that has a chemical affinity for the osmotic membrane covering the organism, but not organotropic or affinity for the osmotic membrane covering the living cells of the body. Salvarsan (606) and its arsenobenzol substitutes have this affinity for the spirochete, and hence its spirocheticidal properties."

### CONGENITAL SYPHILIS: THE INFECTION OF THE FETUS

Congenital syphilis was first described by Ambroise Paré in 1633, but owing to the influence of John Hunter's teaching fell into discredit till the facts were placed on a firm footing.

There is no doubt that congenital syphilis is a more serious infection than primary syphilis, and that the treatment of congenital syphilitics is less satisfactory than in those infected primarily, and Charles Gibbs writes to me that he has never known a positive reaction in a congenital syphilitic child become negative under treatment.

\*Valedictory presidential address delivered before the Harveian Society of London on January 10, 1918. Reprinted by special permission from *The Lancet*, London, Jan. 12, 1918.

There is more than a possibility that syphilis can be transmitted to the third generation. The Venereal Commission reports a case of Dr. Mott's,<sup>2</sup> Mr. J. E. R. McDonagh<sup>20d</sup> describes one in his work on Syphilis, and Mr. C. Gibbs has recently told me of one not yet ready to be published.

There are some who think that direct paternal infection of the ovum by the paternal semen, either at fertilization or after the fertilized ovum has reached the uterus, is impossible. Most authorities think it is possible, but that it is always associated with infection of the mother—i. e., as expressed by Dr. Mott, "that every mother who gives birth to a syphilitic child is herself a syphilitic, and that every syphilitic child has a syphilitic mother."

I believe that not only is paternal infection of the ovum by the seminal fluid possible, but that it is not infrequent, and that the mother may become (1) directly infected either before or with fertilization if she has a genital abrasion or an erosion of the cervix; or (2) indirectly infected during the pregnancy via the embryo (conceptional syphilis); or (3) there seems evidence to show that in a few cases she may be infected by the spirochetes in a granule stage, as I suggest later, and that these may develop into the mature organism after pregnancy.

More usually, however, the embryo is infected by the already infected mother, either by the infection of the ovum whilst in the Graafian follicle as part of the generalization of the disease, or after fertilization when burrowing in the uterine mucosa,\* or by transplacental infection. Sometimes both father and mother may infect the child. Dr. Mott<sup>6</sup> in his article on "Syphilis of Nervous System" in the first and second edition of "Syphilis" an article to which I shall often refer, says:

In an overwhelming number of cases of heredo-syphilis the transmission of the disease to the offspring is directly attributable to the father. The woman in the majority of cases is infected by the man before conception or in conception, so that the child in such cases may acquire the virus from both father and mother. This is termed "mixed transmission."

It is possible that some very early abortions may be the result of paternal infection of the ovum, and that the woman may have

\*In this connection I would draw attention to the researches of Dr. Louise McIlroy,<sup>3</sup> Beckwith Whitehouse,<sup>4</sup> and Carl H. Browning<sup>5</sup> on the incidence of syphilis as shown by positive Wassermann reactions in 50, 44, and 59 per cent, respectively in women suffering from chronic metritis.

escaped infection owing to the expulsion of the ovum very soon after its fertilization and infection,<sup>2</sup> before there is any true fetal circulation.

Cases have been described by Howard Kelly<sup>7</sup> and J. W. Ballantyne<sup>8</sup> where the apparently healthy wife of a syphilitic father has had frequent abortions, but after antisyphilitic treatment of the father alone, the subsequent pregnancies have gone on to the full term and healthy children have been born. This view is also taken by C. F. Marshall and quoted by H. Russell Andrews.<sup>9</sup> Marshall further says that a woman may bear a syphilitic child to a syphilitic father, and that her later children born to a second nonsyphilitic husband, are not syphilitic.

I express no opinion on this point.

There is much evidence<sup>10</sup> that infection can take place by the semen, "although all the other secretions in the body are absolutely normal" and that "the living organism may remain latent for a long time, consequently the sperm may be infected long after the primary infection." I understand that there is difficulty in demonstrating mature spirochetes in seminal fluid.

The spirochete in syphilitic women has been found in the female ovum, for Dr. Mott<sup>6a</sup> says:

Seeing that Levaditi, Bab, and others have seen spirochete in the ova it is possible that the syphilitic contagion may remain in a resting intracellular stage, but when the ovum escapes and is fertilized the syphilitic virus again becomes active, although its virulence is greatly modified and attenuated.

### *Syphilis as a Cause of Antenatal Death*

Syphilis is most contagious in its earliest stages, becoming less virulent in each successive year. Dr. Mott<sup>6b</sup> has shown that—

Syphilitic mothers at first suffer miscarriages with dead children, then have stillbirths, then diseased children dying in early infancy, and eventually may have children showing no signs of disease, some of whom may become general paralytics at puberty, or in early adolescence.

And he goes on to explain that this usual sequence of events is due to antibodies being formed in the body of the mother which modify the virulence of the organism.

The percentage of intrauterine deaths from syphilis is variously estimated, though most observers agree with Mrs. Scharlieb who stated at the Royal Commission on Venereal Disease that syphilis is the commonest cause both of abortions and stillbirths.

Lady Barrett, at the same Commission, said that probably 33 per cent of all stillbirths are due to syphilis. Dr. Russell Andrews says that nearly 50 per cent of syphilitic fetuses are stillborn, and of those born alive 75 per cent die within the first year, most of them during the first few weeks of life. Dr. E. W. Hope, medical officer of health for Liverpool, has pathologic proof that 16 per cent of stillbirths are syphilitic.

Hochsinger's<sup>11</sup> figures are well known. Since 1869 he kept under observation 134 women who showed no signs of syphilis but had given birth to syphilitic children on 569 occasions. Of these, 253 children were stillborn (44.4 per cent) and 316 were born alive. Of these latter, 263 were syphilitic and only 53 apparently healthy. Of the 263 syphilitics, 55 died before the fourth year. These are appalling figures.

Drs. Holt and Babbit<sup>12</sup> had 429 stillbirths (4.29 per cent) in 10,000 confinements at the Sloane Hospital, New York. Of these stillbirths, only 9 per cent were syphilitic, but no recognized cases of syphilis were admitted into hospital.

Dr. Whitridge Williams,<sup>14</sup> in his similar series of 10,000 cases in Johns Hopkins Hospital, had 705 deaths of children between the seventh months of pregnancy and 14 days after birth, and of these 186 (26 per cent) were syphilitic. There were also 164 definite syphilitic infants who survived, and 53 of the "unknown" cases were macerated fetuses which are now known to be usually syphilitic. He therefore estimates that the cases of syphilis were 4.1 per cent of the total births and 32 per cent of the total deaths.

My own opinion is that in city populations about 25 per cent of stillbirths and abortions are due to syphilis. In rural districts the proportion is probably much less, and it is hardly likely that the average loss during intrauterine life and during the first 14 days after birth would be more than 15 or 20 per cent.

I have elsewhere<sup>28</sup> estimated from numerous local and professional calculations made all over the world that, in addition to the total stillbirths which are known to be 3 per cent of the total births, there are about four times as many miscarriages and abortions in the preceding seven months of gestation. This estimate has been provisionally adopted by Sir Arthur Newsholme, medical officer of health to the Local Government Board, and would, if correct, have represented a loss of 138,000 potential lives in England and Wales during the year 1914.

If 20 per cent of these fetal deaths are due to syphilis, it would mean that in England and Wales about 27,000 deaths occur annually in the antenatal period and in the week following from that cause.

The next largest causes of stillbirth are from difficult and pro-

longed labor, variously estimated as from 17 to 45 per cent of the total stillbirths, and from toxemia 6 to 14 per cent. The percentage of abortions and stillbirths is twice as large in unmarried women, and about 50 per cent of these are due to syphilis.

Dr. E. W. Hope, medical officer of health for Liverpool, states that in two large Poor-law establishments in that city the stillbirths among illegitimates were 64 per 1,000 births, as compared with 30 in legitimate births, and 75 per cent of these were due to syphilis, toxemia, antepartum hemorrhage, and dystocia.

As showing what may happen in fresh soil where syphilis was previously unknown amongst the natives, Dr. A. R. Cook, of Uganda, in 1912-14, where there was a terrible outbreak of syphilis, says that out of 40,000 consecutive native dispensary patients, 22 per cent suffered from venereal disease, and that 70 per cent of the children born either died from premature birth or were stillborn or died in the first week after birth from the effect of syphilis.

### *Syphilis in Macerated Stillbirths*

Tissier found evidence of syphilis in 99 out of 155 macerated fetuses and Boissard found that 95 per cent of all macerated fetuses were syphilitic.

Dr. Eardley Holland,<sup>15</sup> who is reporting to the Local Government Board on this subject, found the spirochete in 6 out of the first 7 stillborn fetuses examined and in 12 out of the next 18.

Weber<sup>16</sup> found spirochetes in the organs of 84 per cent of macerated fetuses born in the later months of pregnancy. My colleague, Dr. T. W. Eden, says that in these cases "the *Spirochete pallida* is found in the fetal lungs in 87 per cent, pancreas 80 per cent, skin 66 per cent, suprarenals 64 per cent, spleen 62 per cent, liver 59 per cent, kidneys 54 per cent, but it is easiest to find it in the liver and spleen."

### THE WASSERMANN REACTION IN PREGNANT WOMEN AND NEWBORN LIVING SYPHILITIC CHILDREN

Clinically syphilitic mothers give a positive reaction, even during pregnancy, but some pregnant women are negative even when they are gravid with a syphilitic fetus. Syphilitic children are often negative at birth and for some weeks afterwards.

In a recent letter to me Dr. Mott states that apparently healthy and apparently immune pregnant women who give birth to a syphilitic child "give a positive reaction almost as frequently as the average mother of syphilitic children, and that even if negative when tested, would at one time have been positive." He quotes Knöppelmacher and Lehndorff,<sup>17</sup> who found "that of 91 apparently not syphilitic mothers of congenital syphilitic children, 54 (59.3 per cent) gave a positive reaction, whilst in 25 mothers with certain syphilis there was a positive reaction in 18 (72 per cent), a difference of only 12.7 per cent. These observers also found



that though 90 per cent of the mothers of syphilitic children gave a positive reaction a few months after parturition, only 50 per cent are positive some years afterwards, and 10 per cent of these mothers not only gave no reaction *immediately* after parturition, but remained negative."

Weber<sup>16</sup> states that in most cases in which the mother has presented a true Wassermann reaction he has found spirochetes in the maternal part of the placenta. Trinchese<sup>15</sup> states that spirochetes can usually be found in the center of the villi of the placenta if present in the fetal organs, but are found also in the intervillous maternal spaces and in the epithelium of the villi, showing that they can pass from the maternal to the fetal blood stream and vice versa.

If it could be shown that, in those cases in which an apparently healthy mother bears syphilitic children and yet presents a negative Wassermann reaction spirochetes are only found in the fetal part of the placenta, it would explain much that is obscure.

A. Shillitoe<sup>19</sup> says: "Many women with syphilis will give a negative reaction during pregnancy and positive after delivery."

J. E. R. MacDonagh<sup>20</sup> says: "Broadly speaking, the sera of women during the child-bearing period have a tendency to give negative Wassermann reactions. When the mother and embryo are infected by the contaminated semen the Wassermann reaction is often negative." He has "frequently had cases in which the mother has given birth to an undoubted syphilitic infant and yet her blood has given a negative reaction. Pregnancy no doubt retards or prevents the development of the *Leucocytozoon syphilidis* for the time being."

He continues: "Some time after a pregnancy, should another not supervene, or after the child-bearing period is over, the reaction frequently becomes positive. In some cases repeated pregnancies have undoubtedly resulted in a spontaneous cure of the disease."

In view of my suggestions regarding the action of the chorionic ferments in pregnancy these are especially interesting words.

On the same page he says: "Syphilitic infants born without symptoms of the disease may not give a positive reaction till symptoms appear."

"Commiskey<sup>21</sup> examined 1,822 women and 1,074 infants. Eight per cent of the mothers gave positive results, and 11 mothers who gave negative reactions had children who gave either positive or doubtful reactions. Eighty-two per cent of the women with positive reactions had no history or evidence of disease, yet their previous history showed that 33 per cent of the multiparæ had previous abortions, miscarriages, or stillbirths. The findings in infants would appear to be irregular and generally negative, irrespective of the findings in the mother, and might remain so for years. The death rate amongst children in the first ten days of life was found to be four times greater in those of Wassermann positive mothers than when the mother and child were negative."

Henry Head and E. G. Fearnside<sup>22</sup> describe two cases where there was a negative Wassermann reaction in the serum and a positive reaction in the cerebro-

spinal fluid, and Dr. Mott tells me that this occurs in about 1 per cent of cases of syphilis of the nervous system.

A positive Wassermann reaction does not prove infectivity in a man, neither does a negative reaction in a husband prove that he can not infect his wife or child, for the seminal fluid, as already stated, may long remain infective, as in the following cases:

A man had syphilis six years before marriage and was well treated with mercury for three years, and was negative on two occasions some months before marriage. His wife had two stillbirths at full time, 1 and 2½ years after marriage. Three years after marriage the apparently healthy wife consulted me, desiring to have a living child. After consultation with my colleague, Mr. Charles Gibbs, they each had a Wassermann test, and the husband was found to be still negative, but the wife strongly positive. Both are now being treated by Mr. Gibbs.

I hope my suggestions will help to explain some of the unexpected variations in Wassermann reactions during and for a short time after pregnancy.

#### PROBLEMS STILL REQUIRING EXPLANATION

I want particularly to draw attention to some of the problems which have not yet been fully explained.

*Problem 1.*—Why are some women, gravid with a syphilitic child, negative during their pregnancy and for some time afterwards? This fact was not expected when the Wassermann test was discovered.

*Problem 2.*—A congenitally syphilitic child (born of such a mother) is often also negative at birth, and for some weeks or months afterwards, and may even show no clinical evidences till puberty.

*Problem 3.*—Why are spirochetes almost always absent in the tissues of abortions even in abortions which are prior to or intervene between stillbirths of women known to be syphilitic, or in whose stillbirths spirochetes are found?

*Problem 4.*—Colles' Law.

#### LIFE HISTORY OF THE SPIROCHETE PALLIDA

Before pointing out possible explanations of these problems I must first allude to the results of some researches into the biology of the

*Spirochete pallida* which have been recently described and which seem to me to have important bearings on the points at issue.

To begin with it appears to be still debatable whether the *Spirochete pallida* is a protozoon or a bacterium, whether it is possible that spores can occur or not.

The general view is that the organism is more akin to a bacterium, but it may prove to be in a class by itself. Most observers in this country have failed to be convinced by McDonagh as to the part that sexual "spores" play in the biology of *Spirochete pallida*. McDonagh<sup>20b</sup> tells us that the life-cycle of syphilis commences with a "spore," whilst the mature spirochetes are responsible for the symptoms.

Many observers have, however, described "granules" which are derived from the breaking up of the spirals of the spirochete and which are able under certain conditions to eventually develop into the mature *Spirochete pallida*. The granules are, therefore, spirochetes which are temporarily in a granule stage, in which stage they remain latent or biologically inactive for varying periods. I believe they are definitely infective agents capable of themselves eventually becoming mature spirochetes and may even prove to be infecting agents in some primary infections as well as in congenital.

Dr. Mott<sup>6c</sup> quotes the observations of O'Farrel and A. Balfour, which show "that the injection of salvarsan has the effect of causing a shedding of granules, but that this occurs also independently of the action of any drug."

These authorities consider "that this discharge of granules is protective, undertaken by the spirochetes with a view to prevent their total extinction, the granules being of the nature of resistance spores, the further history of which is unknown, but which, so far as those derived from *Spirocheta pallida* are concerned, doubtless play an important part in relapses and in the later manifestations of syphilitic infections."

Dr. Mott also quotes Noguchi,<sup>6c</sup> who has observed "that in pure cultures of *Spirochete pallida* under certain conditions enormous numbers of minute granules occur, and that from these granules, after transference to a passive culture medium, spiral forms again sprout out. J. E. R. McDonagh and E. H. Ross have each described an intracellular form (leucocytozoon) and a complete sexual cycle of development of the *Spirochete pallida*."

Dr. Mott also says that "the researches of Leishman<sup>6d</sup> on the spirochete of tick fever suggest the possibility of an intracellular phase of the spiral organism and its existence in the form of infective chromidian granules. Moreover, in support of this hypothesis I may mention that Neisser, in his experimental investigations on apes, has observed that the tissues of infected animals in which no spirochetes were demonstrable could nevertheless be used effectually for in-

oculation. The spirochete may be one form of the syphilitic organism, but there may be other minuter stages analogous to the spores of bacilli. These chromidian granules are contained in the *Spirochete pallida*, and in all probability serve a similar function to the nucleus in more highly developed unicellular organisms; consequently, where the mother escapes infection by the parasitic organism, and the offspring alone is infected by it, there are two possible explanations:

“(a) The head of the spermatozoon is infected by a hypothetical syphilitic chromidian granule, which may subsequently multiply and produce the syphilitic lesions;

“(b) If the specific organism never undergoes any modification or metamorphosis and only multiplies by longitudinal or transverse fusion, the explanation of infection would be that spirochetes contained in the sperm may remain alive in the uterus and gain ingress to the developing embryo without infecting the maternal uterus.”

It is believed by Dr. Mott<sup>6a</sup> and others, that the *Spirochete pallida* does undergo some modification, “so that there is a biological difference between the spirochetes of general paralysis and tabes and those of primary syphilis,” but “it is unexplained when, where, and how this change has come to pass,” or why the incubation or latent period should be so prolonged.

In discussing congenital syphilis as regards the sequence of abortions, stillbirths, and live children who are apparently healthy Dr. Mott<sup>6f</sup> says:

“The facts show that antibodies are being continually formed in the body of the (pregnant) mother which kill off the organisms as fast as fresh broods are formed; but with each development of spirillolytic antibodies the organism is modified as regards virulence, so that the tissues of the living offspring are eventually able to cope with the disease by the same process of antibodies and spirillolysis;” and he adds that “just as the pneumococcus or tubercle bacillus may remain quiescent in the body until some depressing or devitalizing condition arises, when they take on an active growth, so it is possible that the spirochete, or a granular antecedent form, may remain latent for many years.”

Taken as a whole, these observations seem to show that when attacked by salvarsan, and probably other drugs, antibodies or toxins, the spirals of the *Spirochete pallida* may break up into granules, which may for a time remain latent and then, unless themselves destroyed by the same agents may develop into mature spirochetes under other circumstances at some later date.

If congenital syphilis is to be checked before it destroys the embryo it must be dealt with locally at its source, and from the very first days after fertilization and infection.

Although antenatal death of the fetus from syphilis is so frequent, I have always found it difficult to understand how such delicate cellular embryonic tissue can ever resist early infection, and what influence or substance it is which is able so often to arrest the progress of the disease in both mother and child during pregnancy.

Great changes go on in every organ of the body, including the ductless glands, during a healthy pregnancy, even so distant and apparently unrelated an organ as the pituitary gland developing special cells, called by Professor E. A. Schäfer "pregnancy cells." These endocrine organic changes no doubt involve altered internal secretions, and doubtless have uses and results, but they take much time to fully develop, especially in the fetus, and can have no part in the early destruction of the spirochete.

#### SUGGESTED ACTION OF THE CHORIONIC FERMENTS

In my evidence before the Royal Commission on Venereal Diseases<sup>23</sup> (on March 9th, 1914), I ventured to explain the latency of syphilis during pregnancy by suggesting that the chorionic ferments might be able to injure or destroy the spirochetes. I also drew attention to the "spores" which Mr. McDonagh<sup>20a</sup> had described, which he believed to be the commencement of the life-cycle of the syphilitic organism, and which he thought were more resistant to the action of salvarsan than the spirochetes. I thought the "spores" might also prove to be more resistant to the action of the chorionic ferments. Even if these sexual "spores" are not confirmed, the "granules," as already described, are clearly the result of the breaking up, spontaneously or otherwise, of the spirochetes. If this can be effected by the action of the chorionic ferments, as I believe it can, syphilitic, as well, perhaps, as other infections such as tubercle, can be arrested, and in syphilis the mature organism can be prevented from passing from mother to child or vice versa, during the pregnancy.

Just before I had finished writing this address I came across the following sentences in Mr. McDonagh's<sup>20b</sup> work on Syphilis (written in 1915) which show that he was being led in the same direction as myself, though he does not state that he has reached the same or any conclusion. He says:

The later manifestations of syphilis in women are very much milder than in men; in women who are bearing children the symptoms are even milder still. From these facts one is tempted to conclude that the serum of women contains more natural protective substances than the serum of men, and that these protective substances are still further increased during pregnancy.

I believe that the chorionic ferments will be proved to be these protective substances, as I suggested in 1914. Under normal circumstances the ferments of the chorionic villi are intended for trophoblastic purposes in order to facilitate the burrowing of the fertilized ovum into the uterine mucosa at the placental site, and to promote the formation of nutritive blood-spaces by destructive action on maternal blood-vessels. The so-called "syncytial toxins" are produced by the action of the ferments upon the maternal tissues. These are controlled or neutralized by so-called syncytio-lysins or by maternal antibodies, and it is believed<sup>24</sup> that if the syncytio-toxins are not sufficiently antagonized by these antibodies in the maternal tissues toxemia results, and may be fatal to both mother and child.\*

The intimate relations between the interdigitating fetal and maternal portions of the placenta are such that the chemical bodies formed by the action of the syncytial ferments upon the maternal tissues penetrate easily through the thin physical barrier between mother and child, so that spirochetes in both can be similarly affected.

This thin physical barrier consists of the cells of the syncytium, and of Langhans's layers, and of the delicate walls of the small vessels on either side of these structures. It is through this maturing physical barrier that the villi can absorb from the maternal tissues all that is required for the growing embryo. This includes nourishment, and interchange of gas, oxygen, and carbon dioxide, between mother and child, from the time when the ovum is only 2 mm. long.

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\*Pregnancy toxemia may take numerous forms, amongst which may be named pernicious hyperemesis, albuminuria, eclampsia, acute yellow atrophy of the liver, toxic diabetes, toxic chorea, and insanity of pregnancy. Nothing is known of the exact causation of these various types of toxemia. It may be due to the course taken by toxic chorionic emboli, formed sometimes of a whole villus, as has been found postmortem; by a varying or abnormal chemical constitution or excess of either syncytio-toxins or syncytio-lysins; or the type of toxemia may be due to some functional or structural condition of one or more of the maternal organs, so that they are the more easily affected by the current toxin.

It has recently been proved that the infants of mothers who have died from eclampsia may develop similar organic changes to those found in the mother's organs, especially in the liver and kidneys.

The chorionic ferments would be more successful in their action on the spirochete, both in its mature and its granule stages, if the embryo was infected by the father's seminal fluid, for it would probably be a single infection. On the other hand, if the mother is already syphilitic, spirochetes would be able to invade the fetal tissues throughout the whole of the pregnancy, and the ferments might easily fail to granulose them all.

If the mother becomes infected at the same time as the ovum her spirochetes might only become available in a few weeks but would then continuously invade the physical barrier between mother and child, even though the ferment derivatives had destroyed the initial paternal infecting agents.

Abderhalden<sup>25</sup> has demonstrated the constant presence of these ferments, capable of splitting up placental albumins and placental peptones, from the sixth weeks of pregnancy to 10 or 15 days after delivery.

Herbert Williamson<sup>26</sup> agrees with Abderhalden that the early and constant presence of these ferments has provided us with a reliable method of serum diagnosis of pregnancy. Abderhalden also states that a definite maternal antibody can be demonstrated between the sixth and the fourteenth week of pregnancy, after which it disappears. This is at a time when the trophoblast is most actively engaged in invasion and destruction of the maternal tissues. He says this controlling antibody can be demonstrated by a complement-fixation test and a technic similar to that of the Wassermann test for syphilis, and Williamson suggests that the explanation of the positive reaction under both circumstances may be the outcome of a somewhat similar destructive action of both the chorionic villi and the spirochete on the maternal tissues.

It will, I think, be found that these chorionic ferments have as destructive an action on the spirochete as on the local, probably prepared, maternal tissues, differing therefore in this latter action from that of salvarsan, which, while able to act chemically on the osmotic membrane covering the spirochete, has no affinity for the membrane covering the living cells of the body.

I believe that not only can the ferments break up the spirochetes into granules, but that the resulting granules can in most cases, by the continued action of the ferments, be kept inactive, and powerless to develop further during the pregnancy. The ferments may even be sometimes able to destroy the granules also.

After pregnancy, in the absence of chorionic ferments, which Abderhalden<sup>25</sup> says can be demonstrated in the maternal blood up to the fifteenth day of the puerperium, the granules, if still present,

may again become biologically active and develop into the mature organism.

#### CONSIDERATION OF THE FOUR PROBLEMS

Now how do these suggestions explain the four problems named?

##### *Problem 1*

*Why may a pregnant woman, who in due course either has a still-born or a living syphilitic child, have a negative Wassermann reaction during her pregnancy, and for some weeks afterwards?*

If a woman is directly infected before or after conception her Wassermann reaction would be positive both during the pregnancy and afterwards, whether the clinical evidences are well marked or slight.

I believe this negative reaction can only occur in cases where the ovum has been infected by the father's seminal fluid, either at fertilization, or after the fertilized ovum has reached the uterine mucosa, and where the mother has hitherto escaped direct infection. In this case the chorionic ferments may break up the infecting spirochetes, if present, into granules; if, however, the ovum is infected by the semen it is probably infected by granules, as the mature spirochete is longer than the head of the spermatozoid. Several granules could be conveyed by a single spermatozoon.

The granules in the fetal tissues would be kept biologically inactive, or "latent" by the continued action of the chorionic ferments, and in that case would not develop into spirochetes during the pregnancy. If so, the mother could only be infected by the granules.

After the pregnancy, 15 days after, according to Abderhalden,<sup>25</sup> all trace of chorionic ferments would have disappeared, and if granules were present in the maternal placenta or in the shreds of fetal placenta which would remain adherent to it at birth, they would develop into spirochetes.

At the end of some weeks of incubation, or after a longer latent period, the woman's reaction might become positive owing to enough antibodies being produced in her body to excite a general reaction in her tissues and blood.



*Problem 2*

*Why are some syphilitic children negative at birth, and for some time afterwards?*

Dr. Mott's<sup>27</sup> explanation is that—

The negative reaction of the blood at birth and for some weeks after does not show that the infection did not take place while the child was developing in the mother's womb or during birth; the child might be born looking healthy, and it would not show signs of disease until the spirochete had become generalized by the blood and lymph streams in all the organs and tissues of the body. The blood reaction is not shown until about six weeks after infection—that is, when the spirochetes have multiplied sufficiently in the body to have produced enough toxins to excite a general reaction of the blood and tissues. It comes just before the secondary rash appears; consequently the child might be infected during the last month of pregnancy or during its passage through the maternal genital structures at its birth.

This statement does not explain how antibodies can be thrown out in sufficient quantities in the minute embryo to resist or destroy the syphilitic infection and prevent it reaching the mother's tissue. Some other chemical agent, which must be in action at the very beginning of pregnancy and throughout its whole duration, seems to me to be required.

I believe the chorionic ferments fulfill this function. It seems probable that children who are negative at birth are the children of mothers who are negative during pregnancy and for some weeks afterwards in cases where the ovum is primarily infected by paternal semen at or soon after fertilization. In such cases, if the paternal semen has infected the ovum by spirochetes, they are broken up by the chorionic ferments into granules, or granules may be the infecting agents, carried by the spermatozoid. In either case the granules may be prevented from further development till after the child's birth. At a variable time afterwards, when chorionic ferments are absent, spirochetes develop, antibodies are formed, and the reaction becomes positive. The only difference, in fact, in the resistance-environment of the child before birth, when its infection is latent, and after birth, when syphilis becomes active, is the absence, in the latter stage, of the protective ferments of the chorionic villi.

It is even possible that during the pregnancy of a previously syphilitic woman the chorionic ferments might prevent her spiro-

chetes from invading the fetal tissues, in which case the mother would have a positive reaction and the child after birth a negative. This would be a strange combination of Wassermann reactions, but Commiskey<sup>21</sup> already quoted, says:

The findings in infants are irregular, but they are generally negative, irrespective of the findings in the mother, and might remain so for years.

It is difficult to explain cases of new-born children who remain negative for more than the normal period of incubation, for I would remind you that Dr. Mott has, as you are well aware, published many cases of juvenile general paralysis and of tabes occurring in children who are "apparently" healthy in mind and body up to the age of puberty or early adolescence. I can get no information as to how long such children may remain negative after birth or how long they may have become positive before the symptoms of their nervous infection becomes evident, but such information would prove valuable and could readily be obtained if some of these "apparently healthy" children could be kept under occasional observation till tabetic symptoms appeared. McDonagh,<sup>20c</sup> however, says that—

Even if a syphilitic child develops no symptoms, as a rule a negative Wassermann reaction obtained soon after birth usually becomes positive about the sixth month.

### *Problem 3*

*Why are spirochetes so rarely found in abortions, even though alternating between stillbirths in whose tissues they are swarming?*

One result of this fact has been that some observers, failing to find the spirochete, do not believe that the early abortions of syphilitic women are due to syphilis.

Thus Frantz Weber<sup>16</sup> has investigated a series of 300 abortions the mothers of which showed no clinical evidence of syphilis. He tried the Wassermann reaction in 67 of these women, and in 35 (52 per cent), where abortion had occurred before the sixteenth week of pregnancy, reaction was uniformly negative, and no spirochetes were found in the embryo; in 32 cases between the sixteenth and twenty-eighth week 12 mothers gave a positive reaction, and spirochetes were found in 9 fetuses (25 per cent).

As already stated, F. Weber found that spirochetes were present in 84 per cent of macerated fetuses after the twenty-eighth week.

It is not stated whether the abortions were from the same women who were delivered of macerated fetuses, which is an important omission. Eardley Holland is reporting to the Local Government Board on this subject, and his views on the point will be awaited with interest.

It has been suggested that the reason why spirochetes are not found in abortions of the first dozen weeks of pregnancy is because the circulation is not sufficiently developed; but Professor D. Waterston writes that "in a human embryo under 3 mm. in length and *under three weeks* old, he found a well-developed primitive heart and a complete system of arterial and venous channels in its body." This evidence seems to negative the suggestion.

I would suggest that if the chorionic ferments had been able to granulose any spirochetes from either father or mother before they could infect the ovum no spirochetes in an early abortion would be discovered. Later on in pregnancy maternal spirochetes might succeed in infecting the fetus in spite of the ferments, and the child would be stillborn with many spirochetes in its tissues, or be born alive a congenital syphilitic.

There may also be some significance in a coincidence I have noticed. Comparing Weber's<sup>16</sup> statement that no spirochetes were found before the sixteenth week, and only in 25 per cent up to the twenty-eighth, there is Abderhalden's<sup>25</sup> statement that a definite maternal antibody is detectable only between the sixth and fourteenth week, after which date it can not be demonstrated. Is this maternal antibody (? otherwise called syncytio-lysin) the main agent of spirillolysis during the weeks when the trophoblast has reached its maximum development and the invasion and destruction of maternal tissues are greatest?

It is quite likely that granules, resulting from the spirillolytic action of the chorionic ferments upon the spirochetes, may be found, if carefully looked for, in the embryonic tissues of these early abortions.

#### *Problem 4*

#### *Colles' Law*

Colles' original statement was that a woman who gives birth to a syphilitic child does not get infected by that child after its

birth, whilst the child can infect another woman—e. g., by a chancre on the nipple. Colles himself made no attempt to explain his statement, but many theories have been built on this dictum.

The *words* of the "Law" as originally stated still hold good, and both Sir Jonathan Hutchinson and Fournier have stated that they have never met with an exception to it.

I am only concerned with the "Law" in regard to my suggestion.

The general view now held to explain the *words* of Colles' Law is that all these women are either infected before or during the course of their pregnancy, and can not therefore be reinfected, "every syphilitic child having a syphilitic mother."

#### *The Woman and Her Child under Colles' Law*

If the above explanation of the words of Colles' Law be right, the mother's clinical condition would fall into the following groups:

1. Where a *woman* is already syphilitic before her ovum is fertilized. Such a woman would have a positive reaction throughout her pregnancy, and could not be reinfected.

The *child* in this group has already been discussed as one of the possible explanations of a child negative at birth (second case, Problem 2), protected by the chorionic ferments from the mature spirochetes of a syphilitic mother, but infected by the organism in the granule stage, and showing signs of syphilis after birth, when the absence of the ferments allows mature spirochetes to be developed.

2. Where a *woman* has a syphilitic husband who has infected the ovum at fertilization by means of his seminal fluid. In such a case the woman might be either (a) or (b).

(a) Be infected at fertilization or during the course of the pregnancy, the chorionic ferments having failed to protect her from spirochetal infection. She should have a positive reaction.

The *child* of this woman is assumed to be infected by the father's semen before or at the same time as the woman.

As soon as spirochetes become generalized in the woman the embryo or fetus is liable to a mixed transmission, and it is not likely that the chorionic ferments would effectively protect it if the infection were virulent. The fetus would probably be stillborn and premature, or, if it survived it would show signs of syphilis at birth, and

would then, according to the Venereal Commission Report, die within the first week or so. Or,

(b) The *woman* resembles the case under discussion in Problem 1. She is negative during the pregnancy and for a short or longer time afterwards, and I have suggested that, owing to the action of the ferments on the infecting spirochetes, she has been infected only by granules during the pregnancy or when the fetal placenta was separated from the maternal placenta. When her store of chorionic ferments is exhausted the spirochetic granules in her tissues may develop into the mature organism.

The *child* in this sub-group corresponds to the first child under Problem 2, negative at birth but liable to become clinically syphilitic soon after birth when the ferments have ceased to inhibit granule activity, or may remain "apparently healthy" till tabetic signs appear about puberty.

#### *Diminishing Virulence of Infection*

As a rule the tendency is for the virulence of congenital syphilitic infection to get less marked in each successive pregnancy, though often there is much irregularity in these sequences. The above tendency can be explained by the formation of antibodies in the mother, which modify the virulence of the organism and so give the chorionic ferments a better chance of destroying them.

The irregularity of some of these congenital sequences may be due to variations in the action of the ferments, or variations in the antibodies present, or both.

#### CONCLUSIONS

My suggestions seem to point to the following conclusions, some of which are scientific facts, whilst others are nonproved, but I think, logical.

1. The "granules" are the result of the "spirillolysis" or break-up of the *Spirochete pallida*.

2. The "granules" are infecting agents, being, in fact, spirochetes in the granule stage. They are able to develop into the mature spirochete in a suitable environment, or may become biologically inactive and remain latent for short or long periods.

3. Chorionic (syncytial) ferments are present at the point of in-

terdigitation of the fetal and maternal portions of the placenta. Their action is primarily trophoblastic to enable the delicate chorionic villi to penetrate the uterine mucosa and to open up maternal blood-vessels, so that the ovum may find for itself a resting-place with nutritive blood-spaces around it. As a result of the destructive action of the ferments upon the maternal tissues so-called syncytiotoxins are formed, but appear to be at once neutralized by so-called syncytio-lysins. If not thus neutralized, maternal and fetal toxemia may become present.

4. The chorionic ferments (or their derivatives) are suggested as being capable of exercising their destructive properties upon the *Spirochete pallida*, which may either be in the maternal intervillous or fetal intravillous tissues, both of which are in intimate relations with the syncytial cells of the villi whence the ferments arise.

5. This destructive action of the chorionic ferments upon the spirochete breaks it up into granules.

6. I further suggest that during pregnancy it is the continued action of the chorionic ferments upon the granules which may render them latent and biologically inactive, and perhaps in a few cases may destroy them.

7. After the pregnancy, when the chorionic ferments cease to be present in the tissues of the mother and child, the granules, wherever they may be, may develop into mature spirochetes.

8. The success or failure of the chorionic ferments to protect the mother and child from spirochetal infection would depend upon (a) the virulence of the infection, which tends to diminish, owing to the presence of more maternal antibodies, with each successive pregnancy; and (b) upon the source of the infection. Infection is probably most difficult to arrest in a "mixed transmission" or in a true maternal infection, where attempts at infection of the embryo would be constantly proceeding throughout the pregnancy. It is probably least severe and most easily countered by the ferments when the primary infection is paternal, for it may then be a single infection only, and probably not capable of repetition if the primary infection be arrested.

9. The Wassermann reaction of mother and child appears to be negative if infection has been by the spirochetes in their granule

stage so long as the granules remain biologically inactive and the mature organism is absent.

This paper is the result of much thought. It consists of a series of suggestions which appear to me to explain logically some of the difficulties which now prevent a clear understanding of antenatal syphilis. At present very little is certain, and proof is difficult to obtain. Physiologic and pathologic chemistry is but little understood, and the presence of these ferments is difficult to demonstrate; the ferments themselves and the various toxins, lysins, and antibodies are all difficult to isolate and identify; and apparently the chemical constitution of none of them is known.

Tests of all sorts are needed to confirm or disprove my suggestions. I have not even been able to find any expert who has the time to prove experimentally, as suggested by Mr. Charles Gibbs, what is the action of the chorionic ferments upon living spirochetes outside the body. If the ferments could be shown to have a spirillolytic action on *Spirochete pallida* outside the body it would be a scientific fact of great value, though a negative experimental result would not necessarily disprove my suggestions.

Before closing I would like to express my sincere thanks to my colleagues, Dr. F. W. Mott, F.R.S., and Mr. Charles Gibbs, for much kind help and useful criticism.

I only ask that my suggestions may receive your kind and patient consideration.

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## CONCERNING THE COAGULO REACTION IN SYPHILIS

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OWING to the prevalence and economic importance of syphilis and the great advances already made in our knowledge of the serum diagnosis and chemotherapy of this disease, numerous investigators continue to find this infection of absorbing interest and worthy of unremitting research, especially in efforts tending to simplify and standardize its diagnosis by laboratory methods and extend our knowledge of its therapy. Accordingly a large number of modifications of the Wassermann reaction and numerous other reactions of a chemico-physical nature based upon precipitation as those of Klausner, Porges and Meier, Herman and Perutz, McDonagh and others have been advocated, the latest of this class of reactions being that of Bruck<sup>1</sup>, who has described a test depending upon the difference of solubility in distilled water of the precipitates of syphilitic and normal serum resulting from the addition of 0.3 c.c. of 25 per cent nitric acid to 0.5 c.c. of serum, the precipitate of syphilitic serum being regarded as sufficiently less soluble in comparison with that of normal serum to be of practical diagnostic value.

Several years ago another and entirely different kind of reaction was described by Hirschfeld and Klinger<sup>2</sup> based upon the observation that syphilitic serum delays or prevents the coagulation of recalcified oxalate plasma beyond that of normal serum, by inhibiting the production of thrombin through interference with the activity of cytozyme or thrombokinas, represented in the reaction by the salt solution emulsion of lipoids from an alcoholic extract of some tissue. We have found that syphilitic serum undoubtedly possesses this peculiarity and while in our experience, the test in its present state is technically too difficult to gain popularity as a practical aid in the serum diagnosis of syphilis, the reaction possesses considerable delicacy and theoretical importance and particularly in relation to the possible explanation of the phenomena of various immunity reactions

in general and the Wassermann reaction in particular, by the principles of colloidal chemistry.

#### PRINCIPLES OF THE COAGULO REACTION

As stated above this reaction is based upon the following conception of the mechanism of blood coagulation: coagulation is due to the formation of fibrin and fibrin is produced from fibrinogen of the plasma by the action of thrombin (fibrin-ferment). The thrombin itself consists of two substances; namely, (1) the serozyme or thrombogen, which is a protein constituent of plasma and (2) the cytozyme or thrombokinase, which belongs to the group of lipoids, particularly the lecithins, and in the blood is believed to be derived chiefly from disintegrated blood platelets. Ionized calcium must be present before these substances unite to produce thrombin, but the latter can precipitate fibrinogen into fibrin and cause coagulation in the absence of calcium ions, for example, in oxalate plasma.

While the cytozyme is derived chiefly from disintegrated platelets during the coagulation of blood, it may be secured *in vitro* by extraction from almost any cells or tissues by means of alcohol; in Hirschfeld and Klinger's test it is supplied by the ordinary alcoholic extracts of normal tissue used as antigens in the Wassermann reaction. The cytozyme or lipid material is essential in the formation of thrombin and hence in the phenomenon of coagulation; anything tending to interfere with its activity will delay or inhibit coagulation. Hirschfeld and Klinger's reaction is based upon the observation that syphilitic serum when mixed with cytozyme interferes with its activity to a greater extent than normal serum and thereby delays or prevents thrombin production and coagulation. No adequate explanation has been made of the substance in syphilitic serum responsible for this action upon the cytozyme or of the mechanism of its interference; at present syphilitic serum is regarded as possessing the property of destroying cytozyme or rendering it inactive by enmeshing the lipid particles in the globulins of the serum. Because the test is based upon the inhibition of coagulation by interference with thrombin production, the reaction has been named by Hirschfeld and Klinger the "coagulo reaction."

In conducting the test the first phase consists in mixing 0.1 or 0.2 c.c. of treated serum with 0.1 c.c. of varying dilutions of alcoholic extract of tissue (the cytozyme) and allowing the mixtures to stand for

one-half to an hour to permit the inactivation or enmeshing of the lipid particles of the cytozyme by the serum, and particularly if the serum is derived from a syphilitic; calcium chloride and serocym (fresh plasma) are then added as the second phase and the tube stood aside for fifteen minutes to permit the production of thrombin providing cytozyme is available, the amount of thrombin produced bearing a direct ratio to the amount of cytozyme present. The third phase consists in testing for the presence and amount of thrombin by adding a solution of fibrinogen and timing the reaction to determine when fibrin formation or coagulation has occurred. The controls generally coagulate within a few minutes; normal serum may delay coagulation a few minutes longer, while syphilitic serum delays coagulation for a longer period or indefinitely; the reaction, therefore, is a quantitative one. Since solutions of fibrinogen are unstable, a weak solution of oxalate plasma is employed in the last step of the test to measure the amount of thrombin present. The employment of oxalate plasma (Bordet and Delange<sup>3</sup>) has not only the advantage of keeping for a long time, but it also prevents any further formation of thrombin from the moment at which the plasma is added, because the sodium oxalate precipitates the calcium in the form of insoluble calcium oxalate, and the consequent lack of calcium ions renders impossible the further formation of thrombin.

The following schemes present the processes of coagulation, positive and negative coagulo reactions:

#### (1) NORMAL COAGULATION

Cytozyme (lipoids from cells and particularly blood platelets) + serozyme (a protein constituent of plasma) + calcium ions = thrombin (fibrin ferment).

Thrombin + fibrinogen = fibrin (coagulation).

#### (2) POSITIVE COAGULO REACTION

*First Step.* Cytozyme (emulsion of lipoids from alcoholic extract of heart muscle) + heated syphilitic serum = inactivation of cytozyme (probably by enmeshment of lipid particles).

*Second Step.* + serozyme + calcium ions = slight or no thrombin production (due to interference with activity of cytozyme).

*Third Step.* + fibrinogen (in form of oxalate plasma) = delayed or absent coagulation because of insufficient amount or absence of thrombin.

## (3) NEGATIVE COAGULO REACTION

*First Step.* Cytozyme + heated normal serum = slight or no inactivation of cytozyme.

*Second Step.* + serozyme + calcium ions = good thrombin production.

*Third Step.* + fibrinogen (oxalate plasma) = coagulation which may be delayed but not to the extent observed when syphilitic serum is employed.

## PREPARATION OF REAGENTS FOR THE COAGULO TEST

In conducting the coagulo reaction five reagents are employed:

1. The oxalate plasma which is used instead of a solution of fibrinogen in testing quantitatively for thrombin and also in the preparation of serocym.

2. The serocym.

3. A solution of calcium chloride in physiologic salt solution.

4. The cytozyme or alcoholic extract of tissue emulsified in physiologic salt solution.

5. The serum of the patient.

1. *Oxalate plasma* which is used in the preparation of serozyme and in the third step of the test, is prepared as follows:

- (a) In a flask marked with a wax pencil to indicate a volume of 100 c.c. place 10 c.c. of a solution of oxalate prepared of 0.48 gm. sodium oxalate, 48 c.c. distilled water and 2.5 c.c. of a 10 per cent sodium chloride in distilled water.

- (b) With a short, stout sterilized needle secure blood from the external jugular vein of a sheep or goat to the 100 c.c. mark (the first one or two cubic centimeters of blood flowing from the needle should be discarded); with large animals 20 c.c. of oxalate solution may be used and blood collected to a 200 c.c. mark.

- (c) Before collecting the blood the required amount of oxalate solution should be placed in the flask, heated to 40° C. and the interior of the flask moistened with the warm oxalate solution to prevent the condensation of steam from the warm blood during its collection upon the wall of the flask which may result in producing some hemolysis. During the collection of the blood the flask is *gently* shaken to prevent coagulation and everything must be avoided which might favor the formation of thrombin.

- (d) The blood-oxalate mixture is now poured into centrifuge tubes previously rinsed with warm physiologic salt solution and centrifuged

for 15 to 20 minutes; the supernatant fluid is then transferred to fresh centrifuge tubes and again centrifuged for at least 30 minutes at high speed to remove the platelets. The resulting plasma should be absolutely clear and free of hemoglobin; if colored at all it should possess but a yellow shade. A good plasma will keep in a refrigerator fit for use for at least one or two weeks. It is employed as such in the preparation of the serozyme, but in the third step of the coagulo test when it is employed instead of a solution of fibrinogen as a test for thrombin, the plasma is diluted as follows and used in dose of 1 c.c.:

Oxalate plasma .....	1 part	(10 c.c.)
1 per cent sodium oxalate in distilled water.	$\frac{1}{2}$ part	( 5 c.c.)
Physiologic salt solution (0.85 per cent sodium chloride in distilled water)....	5 parts	(50 c.c.)

Not infrequently small coagula appear in the plasma after standing one or two days, caused by small amounts of thrombin produced in spite of all precautions; these may be filtered off through sterile cotton wool.

2. The *serocym* is prepared by recalcifying oxalate plasma as follows:

(a) Place 45 c.c. of fresh oxalate plasma in a small beaker and add 5 c.c. (one-tenth volume) of 1 per cent calcium chloride in distilled water; mix well and place in an incubator for at least fifteen minutes. The plasma immediately becomes turbid and finally coagulates. If the plasma has not coagulated at all or but partially, a few more drops of calcium chloride solution may be added. Occasionally oxalate plasma do not coagulate at all, or but poorly, and particularly plasma which has been left for three days or longer; these can not be used for the preparation of serocym although they may be satisfactory for use in the third step of the test.

(b) The coagulum is now grasped with long forceps and the serocym expressed by pressing the coagulum with a wringing movement. If the plasma coagulates again, the coagulum should be removed again in the same manner as this does not interfere with the quality of serocym. As freshly prepared serocym may contain traces of thrombin it should not be used for at least one or two hours to insure absence of all tendency for coagulation in the serocym.

(c) In conducting the tests the serocym is diluted with five volumes of physiologic salt solution and used in dose of 0.5 c.c. Before being

used a preliminary test must show that it is satisfactory, that is, produce thrombin in the presence of serozyme and calcium as tested by the coagulation of oxalate plasma. This test will be described later.

The preparation of good serocym is the most difficult step in the technic. According to Uemura<sup>4</sup> the bloods of different sheep and goats vary in their field of serocym and if an animal is found unsatisfactory others must be tried. Rabbit blood is generally satisfactory but the yield of serocym small; the blood of guinea pigs, oxen and human beings are likewise unsatisfactory (Uemura). Serozym does not keep well and should be freshly prepared before each lot of tests.

Uemura states that a weak serocym may be improved by diluting it with ten volumes of distilled water and allowing the mixture to stand several hours; to the mixture, which is cloudy, due to precipitation of globulins, is added sufficient 10 per cent sodium chloride solution until it contains 0.8 per cent salt, after which it may be used in dose of 1 c.c.

3. The *calcium chloride solution* is prepared by mixing 5 c.c. of a 1 per cent solution in distilled water with 95 c.c. of .85 per cent sodium chloride in distilled water (designated as physiologic salt solution).

4. The *cytozyme* or lipoids of tissue extracts may be furnished by an alcoholic extract of human beef or guinea pig heart or human liver emulsified in normal salt solution; in our experiments alcoholic extracts of syphilitic liver were generally unsatisfactory. Before using an extract it must be tested to determine its fitness as cytozyme by placing in two test tubes 0.1 c.c. of 1:20 and 1:40 dilutions in physiologic salt solution respectively, and adding to each tube 1 c.c. of the calcium chloride solution, 0.5 c.c. of the serozyme solution and 1 c.c. of the oxalate plasma dilution, employed in the main tests; coagulation should result in from one to three minutes. It is not permissible to use higher concentrations of an extract (as 1:10) because of the alcohol which affects the formation of thrombin. If an extract is too weak to cause coagulation in 1:20 and 1:40 dilutions, it may be concentrated by vaporizing the alcohol in an incubator; weak extracts should not be employed.

In conducting the tests four dilutions of cytozyme are employed in constant dose of 0.1 c.c.; namely 1:40; 1:80; 1:160 and 1:320. As the coagulation time differs with each dilution, four different tests are conducted simultaneously with each serum without greatly increasing

the labor entailed and adding much to the accuracy and ease of interpretation of the results.

5. The *fluid to be tested* is collected as for the Wassermann reaction and must be clear, absolutely free of corpuscles and free of dissolved hemoglobin; if tinged to any appreciable degree with hemoglobin the reaction is disturbed. As serum resulting from spontaneous coagulation is always likely to contain cytozyme, which would disturb the reaction, the sera are heated at 56° C. for an hour to destroy this element; on the other hand sera rich in cytozyme as those secured by breaking up blood clot and those sent in the mails from a distance, usually require heating at 60° C. for an hour. At times even this exposure fails to destroy the cytozyme and autocoagulation occurs, as shown in the serum control of the test.

#### TECHNIC OF THE COAGULO TEST

Before the main tests are conducted certain preliminary tests should be made to determine whether the various reagents are active and satisfactory, as follows:

1. The reagent controls prepared by placing in two test tubes 0.1 c.c. of 1:20 and 1:40 salt solution dilutions of alcoholic extract of heart (cytozyme) respectively, 1 c.c. of calcium chloride solution and 0.5 c.c. of serocym solution; after mixing the contents of each tube and standing aside at room temperature for fifteen minutes to permit the formation of thrombin, 1 c.c. of oxalate plasma solution is added to each and timed with a watch for coagulation which should be complete within three minutes, producing a firm opaque jelly-like mass in each tube. These tests show that the cytozyme in both dilutions, serozyme, calcium solution and oxalate plasma are satisfactory. If coagulation does not result the trouble is usually due to defective serocym or the tissue extract (cytozyme).

2. Positive and negative controls conducted with a syphilitic and strongly Wassermann positive serum and a normal serum respectively, heated at 56° to 60° C. for one hour. These tests are set up after the manner of the main tests, and the tubes containing syphilitic serum should show a delay in coagulation as compared with the normal serum and reagent controls.

The main tests are conducted as follows:

1. Each serum is heated at 56° to 60° C. for one hour.

2. For each serum arrange five small, chemically clean and sterile test tubes in a row; into each of the first four place 0.1 c.c. of 1:40, 1:80, 1:160 and 1:320 salt solution emulsions of cytozyme (alcoholic extract of heart), respectively. The fifth tube is the serum control and receives 0.1 c.c. of salt solution.

3. To each of the five tubes add 0.1 c.c. of heated serum; mix well and stand aside at room temperature for an hour. During this interval the serum is acting upon the cytozyme and in the case with syphilitic sera, the lipid particles of the cytozyme are regarded as enmeshing in the serum globulin, which inactivates or prevents the cytozyme in part or totally from participating in the production of thrombin.

4. To each tube add 1 c.c. of calcium chloride solution and 0.5 c.c. of serocym solution; mix and stand aside at room temperature for fifteen minutes to permit the formation of thrombin according to the amount of available cytozyme.

5. To each tube add 1 c.c. of oxalate plasma solution recording accurately with a watch the minute when oxalate plasma is added; mix and examine each tube every minute for coagulation.

The controls:

6. (a) The fifth tubes of each series are the serum controls and these should remain fluid for several hours at least and usually until next day or indefinitely because they contain no cytozyme which is essential for thrombin formation. Occasionally sera heated at 56°C. contain sufficient cytozyme derived from platelets during coagulation of the blood to produce autocoagulation; a fresh specimen of such serum should be heated at 60°C. for an hour which may destroy the blood cytozyme and the test repeated.

(b) Each dilution of cytozyme (tissue extract) in dose of 0.1 c.c. should be set up without serum (substituting 0.1 c.c. normal salt solution) and show coagulation in from one to six minutes, the higher dilutions requiring more time than the lower.

(c) A positive and negative control conducted with heated syphilitic and normal serum as described above.

#### THE COAGULO REACTION

An accurate record of time in minutes must be kept of each tube of the series and the serum controls until the tubes of normal serum



containing cytozyme and the tubes containing all reagents except serum (the cytozyme controls) show coagulation; after this each tube should be examined at close intervals so that a record of time in minutes required for coagulation in each tube may be recorded. The serum controls should not coagulate at all.

The normal or nonsyphilitic sera usually coagulate within ten minutes, but this interval may be shorter or longer (an hour or more) depending upon the quality of cytozyme, serozyme and oxalate plasma. Strongly syphilitic sera delay coagulation for considerably longer periods and particularly in those tubes containing the higher dilutions of cytozyme; weakly syphilitic sera delay coagulation only slightly beyond the time required for coagulation with normal serum. The coagulo test is, therefore, a distinctly quantitative test and it is highly desirable to work with five or more sera at one time and include a weakly positive control in addition to a strongly positive one, as aids in the interpretation of results. *No standard or definite time can be laid down for the coagulation of normal or syphilitic serum* inasmuch as the time varies with each new lot of serozyme and oxalate plasma and the strength of the cytozyme; each experiment or set of tests must be set up with normal or negative and positive serum controls and the results of the reaction with the remaining sera judged solely upon the time required for coagulation with the particular controls employed. Examples of the variation in time required for coagulation with different lots of serozyme are amply shown in the controls of tests shown in Tables I and II.

Coagulation is indicated by the development of a firm jelly-like coagulum in the tubes. It is convenient to express the results with  $\pm$ , + and ++ signs;  $\pm$  indicating slight delay in coagulation as two or three minutes, + a delay of five to ten minutes and ++ a longer delay or entire inhibition of coagulation (fl.=fluid).

After observing the results for an hour or two the tubes may be left standing in the laboratory overnight and inspected again the following morning.

An inspection of Tables I and II will readily show the time required for coagulation with a number of positive and negative sera and a comparison of the readings of the coagulo and Wassermann reactions.

TABLE I  
RESULTS OF WASSERMANN AND COAGULO REACTIONS

SEEA	WASSERMANN REACTION			COAGULO REACTION**				SUMMARY OF RESULTS	
	C.H.*	S.	A.	1:40***	1:80	1:160	1:320	Serum control	
Control with syphilitic serum	+++	+++	+++	fl.	fl.	fl.	fl.	fl.	+++
Control with normal serum	-	-	-	6	29'	60'	70'	fl.	-
Control with extracts alone	-	-	-	3½'	3½'	4'	5'	fl.	0
Secondary syphilis	+++	+++	+++	65'	65'	fl.	fl.	fl.	+++
Secondary syphilis	+++	+++	+++	fl.	fl.	fl.	fl.	fl.	+++
Secondary syphilis	+++	+++	+++	15'	16'	fl.	fl.	fl.	+++
Tertiary syphilis	+++	±	+++	6'	fl.	fl.	fl.	fl.	+++
Tertiary syphilis	+++	+++	+++	11'	fl.	fl.	fl.	fl.	+++
Tertiary syphilis	+++	±	+++	fl.	fl.	fl.	fl.	fl.	+++
Secondary syphilis	+++	+++	+++	27'	36'	fl.	fl.	fl.	+++
Secondary syphilis	+++	+++	+++	15'	fl.	fl.	fl.	fl.	+++
Secondary syphilis	+++	+++	+++	6'	20'	25'	fl.	fl.	+++
Secondary syphilis	+++	+++	+++	15'	16'	fl.	fl.	fl.	+++
Secondary syphilis	+++	+++	+++	8'	20'	fl.	fl.	fl.	+++
Latent syphilis	+++	+++	+++	5'	6'	7'	8'	fl.	+++
Tertiary syphilis	+	-	-	5'	7'	15'	15'	fl.	+
Doubtful diagnosis	-	-	-	5'	10'	10'	fl.	fl.	-
Tertiary syphilis	±	-	±	13'	20'	fl.	fl.	fl.	±
Nonsyphilitic	-	-	-	5'	6'	7'	8'	fl.	+
Nonsyphilitic	-	-	-	5'	5'	10'	20'	fl.	-

\*C.H., cholesterinized alcoholic extract of beef heart; S, alcoholic extract syphilitic liver; A, acetone insoluble lipoids of beef heart.

\*\*The figures indicate minutes required for coagulation; fl., fluid or absence of coagulation.

\*\*\*Dilution of an alcoholic extract of human heart.

TABLE II  
RESULTS OF WASSELMANN AND COAGULO REACTIONS

SERA	WASSELMANN REACTION			COAGULO REACTION**					SUMMARY OF RESULTS	
	C.H.*	S.	A.	1:40***	1:80	1:160	1:320	Sera control	Wass. R.	Coagulo R.
Control with syphilitic serum	+++	+++	+++	5'	5'	20'	fl.	fl.	+++	++
Control with normal serum	-	-	-	3'	3'	4'	8'	fl.	-	-
Control with extract alone	-	-	-	2'	2'	3'	4'	fl.	0	0
Tertiary syphilis	+++	+++	+++	3'	4'	7'	10'	fl.	+++	±
Secondary syphilis	+++	+++	+++	3'	4'	5'	10'	fl.	+++	±
Tertiary syphilis	+	-	+	3'	4'	5'	8'	fl.	+	-
Latent syphilis	+	-	-	3'	4'	5'	8'	fl.	+	-
Secondary syphilis	+++	+++	+++	3'	5'	8'	20'	fl.	+++	+
Secondary syphilis	+++	+++	+++	3'	4'	8'	9'	fl.	+++	±
Secondary syphilis****	-	-	-	3'	4'	6'	9'	fl.	-	-
Nonsyphilitic	-	-	-	3'	4'	5'	8'	fl.	-	-

\*C.H., cholesterolized alcoholic extract of beef heart; S, alcoholic extract syphilitic liver; A, acetone insoluble lipoids of beef heart.

\*\*The figures indicate minutes required for coagulation; fl., fluid or absence of coagulation.

\*\*\*Dilutions of an alcoholic extract of human heart.

\*\*\*\*After receiving nineteen injections of arsphenamine (arsenohenzol of the Dermatological Research Laboratories).

## PRACTICAL VALUE OF THE COAGULO TEST

Hirschfeld and Klinger<sup>2</sup> have reported tests with 750 sera, finding that the results of the coagulo tests paralleled those of the Wassermann reaction except that the coagulo reaction seemed a little more sensitive. Fränkel and Thiele<sup>5</sup> have reported favorably upon the results of Wassermann and coagulo tests with 70 sera, finding that the coagulo test surpassed the Wassermann in delicacy and particularly in treated and latent syphilis. Cole and Chiu<sup>6</sup> have reported upon tests with 548 sera and 51 cerebrospinal fluids (heated at 58° C. for half an hour and used in doses of 0.4 c.c.) concluding that the coagulo test is quite as specific as, and more delicate than the Wassermann, in cases of treated, latent and cerebrospinal syphilis. A few cases were observed to yield positive coagulo and negative Wassermann reactions; after prolonged and effective treatment, negative results were observed with the coagulo as with the Wassermann reaction. Uemura<sup>4</sup> after examining 500 sera with the coagulo and Wassermann methods found the two tests agreeing in 92.75 per cent of cases; in thirty cases of treated and latent syphilis yielding negative Wassermann reactions the coagulo reactions were positive; in eight cases of syphilis with positive Wassermann reactions the coagulo reactions were negative. Generally considered Uemura found the coagulo test more sensitive than the Wassermann inasmuch as it yielded 7.5 per cent more positive reactions, although he believes that the technic is still too difficult and subject to error and mishap to replace the time-honored and valuable Wassermann reaction.

In our experience with sera from syphilitics in all stages of the disease except the primary stage and with and without arsphenamine (arsenobenzol) treatment we have found the coagulo reaction very delicate and highly specific. No positive reactions were observed with the sera of nonsyphilitic persons. As compared with the Wassermann reaction conducted with acceptable alcoholic extracts of heart muscle reenforced with cholesterin, the coagulo reaction was somewhat less delicate and definite in cases of tertiary, latent and intensively treated syphilis; but usually more delicate and definite than Wassermann reactions conducted with alcoholic extracts of syphilitic liver. In secondary syphilis both the Wassermann and coagulo reactions were uniformly and strongly positive; an examination of Tables I and II will show the varying intervals required for

coagulation with different reagents and how we have found a number of sera to compare in both reactions. We have not submitted cerebrospinal fluids to the coagulo test but Cole and Chiu<sup>7</sup> have examined a large number with satisfactory results.

While the technic of the coagulo test is very simple, the preparation of several of the reagents is difficult and so frequently disappointing in their properties as to constitute an objection to the adoption of the test as a practical aid in the diagnosis of syphilis. The reaction is, however, of great interest and value in relation to the phenomena of several immunity reactions by reason of the principles involved, and certainly worthy of extended study not only for this important reason, but also from the standpoint of a practical test for syphilis. At present we are engaged in experimental studies with the reaction and hope to still further simplify the technic and thereby improve its diagnostic value.

#### SUMMARY

1. The coagulo reaction is based upon the observations of Hirschfeld and Klinger that syphilitic serum inhibits or delays the formation of thrombin and consequently of coagulation, by an inactivating influence upon cytozyme, one of the essential elements in thrombin formation.

2. The reaction has been found a highly delicate and constant characteristic of syphilis, although in our experience slightly less sensitive than the Wassermann reaction conducted with acceptable alcoholic extracts of heart muscle reenforced with cholesterolin.

3. The coagulo reaction is regarded as specific for syphilis, but further investigations with the sera of persons suffering with various other diseases are required before a definite statement is warranted.

4. The preparation of suitable reagents for the coagulo test is at present too frequently disappointing to place the reaction on the basis of a practical routine test for syphilis; it is possible, however, that further experiences will simplify the technic and remove this objection.

5. The coagulo reaction possesses considerable interest and importance in relation to the mechanism of several immunity reactions and particularly complement fixation by reason of the principles involved.

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## SYPHILIS IN DETROIT AS AN ECONOMIC AND SOCIAL FACTOR\*

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A SYPHILOGRAPHER is generally accused of considering the spirochete as the root of all diseases and it will be my endeavor to show a few phases in the course of syphilis—the source of infection, the influence of the spirochete in the limitation of families and the economic loss to the state in caring for those incapacitated by syphilis.

The human race can be divided into three classes with a possible fourth—those who have had syphilis, those who have it, and those who are going to have it—the fourth being the fortunate few who may escape.

In the matter of statistics of any condition the inhabitants of a given city are prone to disregard similar conditions for other cities, and, ostrich-like, think that if their own shortcomings are not uncovered they should be unconcerned about their neighbors'. Then, too, if the economic loss at home, due to the presence of disease is placed (in dollars and cents) before the eyes of the powers that be, it will attract more attention than a similar statement from some other locality.

There has never before been an opportunity of presenting any accurate statistics on this subject and it is only possible now on account of the excellent work being done by the Harper Hospital Social Service Department in locating and following up all cases of syphilis referred to the Department.

The saying "Men may come and men may go, but I go on forever" can apply to the spirochete as well as to the brook, with this addition—that the spirochete has a great deal to do with the comings and goings of men. The prevalence of syphilis is appalling even to those

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\*Read before the Wayne County Medical Society, December 10, 1917.

who come in contact with it daily and after the war it will probably be even more widespread than at present. It has been reported to me on good authority that even now in Australia the school lavatories have been closed on account of the prevalence of syphilis due to the return of infected soldiers from Egypt. As in all widespread diseases, the deserving as well as the undeserving may become affected, and the proportion of innocent syphilitic infections is far greater than is realized.

Syphilis may be transmitted in one of three ways—sexually (including prostitution, clandestine or open, and marital relations), parental transmission and extragenital infection. While statistics of other cities may vary greatly from our own, those affecting ourselves may be accepted as the most important at present. In determining the percentage of the above-mentioned methods of infection, 400 cases of syphilis of all kinds were considered without regard to age, sex, condition of life, etc., and the source of contagion determined as accurately as possible.

It is practically an impossibility to obtain an accurate percentage of the incidence of syphilis in general, but it is admitted that twenty per cent is a fair estimate, though in many localities the percentage would be far greater.

It has always been my contention that syphilis is spread as much by clandestine prostitution as by the inmates of houses and that so much disgrace should not be attached to a syphilitic, as so many cases are innocently infected. I admit I have been greatly surprised to find how large a percentage of innocent infections had occurred among men as well as among women and children. There has been recently considerable agitation here in the demimonde on account of the closure of the houses of prostitution in an attempt to control the spread of venereal disease, but after a careful study of the cases under my care and talking to members of the underworld, I have come to the conclusion that forcible attempts to prevent prostitutes from plying their trade, have not improved matters any, but, if anything, have made prostitution more clandestine than ever and therefore that much harder to control.

In analyzing these 400 cases, they have been classified as to source of infection, (i.e. innocent or illicit), the innocent infections being further subdivided as to the type of marital infection, extragenital



and congenital. The age and sex of cases also were noted. Illicit infections were classified into infections by friends—which would include those girls having an occupation other than prostitution and all those having clandestine relations—and infection by prostitutes, either street-walkers or inmates of houses.

In our department the number of adults would far outnumber the children, being 355 adults to 45 children, or 88.75 per cent to 11.25 per cent. Many children are, however, under treatment in the Department of Pediatrics. Contrary to the opinion generally expressed the proportion of males to females is fairly equal, being 218 males to 182 females. These figures would vary in different cities and in the different clinics in the same cities, depending upon the locality of the dispensary.

Of the 400 cases under consideration, it was found that 212 were infected in an illicit manner (53 per cent), either by friends or prostitutes, while 188 were innocent in the contraction of the disease, a percentage of 47; 101 infections could be traced to friends of the victims, while 111 stated a street-walker or house prostitute was responsible, giving 52.35 per cent illicit infections due to clandestine prostitution.

This high proportion of innocent infections is largely due to the efforts made to find cases in the families of syphilitics—individuals who are apparently healthy but have latent syphilis.

Believing these figures to be true how can one suppose that the enforced suppression of the red light district will affect the transmission of the disease to any appreciable extent? It is common knowledge that many former inmates of houses have taken small apartments in various locations and still continue to entertain their gentlemen friends and are now practicing clandestine instead of open prostitution.

If the disease could be limited to those who contract it illicitly it would be more endurable, but consider that a great many of these illicit infections have infected innocent persons, caused many deaths, and were responsible for some living lives of misery, blindness, insanity or paralysis. Of a total of 188 cases innocently luetic, infected husbands were responsible for 56 per cent (107 cases), 25 (13.29 per cent) contracted the chancre extragenitally; 52 cases (27.64 per cent) were children infected before birth, while in four

cases wives had infected their husbands. These figures show that the males are by far the greatest spreaders of innocent syphilis, 107 cases being males infected by friends or prostitutes, four cases being husbands infected by their wives who had contracted the disease illicitly. How can one doubt the value of venereal prophylaxis after knowing how many innocent victims can be made to suffer through carelessness, ignorance, and prudery?

Of all cases husbands caused 26.75 per cent, 6.25 per cent were extragenital, 13 per cent were congenital, 1 per cent were infected by wives.

Taking the total of all cases the percentages are as follows:

Total cases, 400.	
Of friend infections	101—25.25%
Of prostitute “	111—27.75%
Of husband “	107—26.75%
Of wives “	4— 1%
Of congenital “	52— 13%
Of extragenital “	25— 6.25%

In considering the waste due to syphilis, two different conditions were studied, first, the economic waste due to many syphilitics suffering from paresis, tabes, blindness, etc., being public charges; second, the waste in human lives due to the tendency of syphilis to produce miscarriages, stillbirths, defectives of all kinds, and those in whom the disease is latent, but who would probably develop symptoms at puberty, or following some illness.

Inquiries were sent to a number of institutions throughout the state asking for information concerning the following: Total number of inmates, number or percentage ofluetics, total yearly cost of operation, and cost per patient. Some institutions were able to give only an estimate of the number of syphilitics, stating however, that Wassermann tests would probably show a larger proportion. The percentage of financial waste was computed by taking the percentage of known cases of syphilis. It is true that perhaps many of theluetie cases would be institutional charges irrespective of syphilis, but that would be offset by the fact that the true proportion of syphilitics would be greater than stated, in all probability.

The Michigan Employment Institution for the blind at Saginaw, Michigan, has 100 inmates, 18 per cent of whom are syphilitic. There are no active cases, all syphilitic blindness being in those who have

had syphilis in the past or inherited it. The actual percentage is stated to be higher than the estimate. Syphilis would here cause a loss of at least \$5,400 out of a yearly cost of \$30,000.

The Kalamazoo State Hospital—2,200 patients,—reports 7.5 per cent of syphilis in the insane, 12.3 per cent in general paresis, 3 per cent in maniac depressive insanity, 21 per cent of colloidal gold reactions and 20 per cent of Wassermann reactions being positive. The yearly cost per patient is \$255, or a total waste due to syphilis of \$112,000.

The Newberry State Hospital gives a percentage of 13.2 syphilis (probably too low) with a consequent wastage of \$25,000 per year.

The Michigan Home and Training School at Lapeer, out of 1,459 patients, reports 9 per cent as having a positive Wassermann from + to 4+. As this is not a hospital institution, the percentage would naturally be lower, yet with a yearly cost per patient of \$240, there is a yearly wastage of at least \$31,000 from syphilis.

At the State Psychopathic Hospital at Ann Arbor there were 449 patients examined in 1914-1916, 74 had a positive Wassermann, a percentage of 16.5. Their cost per patient per day is about \$2, their total expense for 1915-16, \$80,000, giving a cost for syphilis of \$13,000.

Traverse City State Hospital in its last report had about 1,600 patients with a death rate due to syphilis of 15 per cent; the percentage of syphilitics would probably be much higher. They had a yearly expense of \$400,000, or at a minimum \$60,000 waste from syphilis.

A recent letter from James Russell, warden of the State prison at Marquette, states that they have 391 inmates, a yearly expense of \$105,000 and approximately 50 per cent are sexually diseased on admittance. He further states:

“From what I have learned about the prevalence of syphilis among men committed to this prison by questioning them and having them examined by the physician when they enter, I think I am safe in saying that fully fifty per cent of them are sexually diseased when they come here. It is a conviction with me that sexual disease contributes largely to the criminality of those men. Because of it many of them come here physical wrecks, and really incapable of earning a living honestly. I recall that last year sixteen young men between

the ages of nineteen and twenty-six were received here within two weeks, and all but one of these were sexually diseased. This indicates to what extent venereal diseases prevail among the youth of the country who are willing recruits for our large and constantly increasing criminal army."

At the Pontiac State Hospital a survey is in progress at present and the latest figures are not yet available.

Out of the 1,498 inmates, 91 cases, 6 per cent, are luetic. A yearly cost per patient of \$225 makes a syphilitic loss of \$22,000. They also state that the actual percentage would probably be much higher as does the county house at Eloise, although the latter estimates 25 per cent as the minimum of their inmates infected with syphilis.

The total loss from these various institutions is thus seen to be well over a quarter of a million dollars annually, and does not include all institutions even in one state, nor does it include the cost due to the treatment of all syphilitics.

The institutional cost for luetics is based on the supposition that the patient would be self-supporting if he were not infected, while the expense to all luetic individuals for proper treatment is incalculable.

Without considering the conditions due to acquired syphilis the abnormal states due to the influence of syphilis in a former generation are numberless. These conditions, while due to syphilis, do not respond readily to antiluetic treatment and are probably due to impaired inheritance and not to the disease itself. The neurologist and internist can tell you more of those conditions than I can.

We were able to tabulate 74 families in which syphilis was present—in three of which no pregnancies had occurred, while the remainder had had from 1 to 12 pregnancies. All statistics relative to children were made on pregnancies subsequent to the luetic infection as some of the women had been twice married or had previously had healthy children before infection. In 71 families pregnancies to the number of 253 were recorded, of which 158 children are living at present, while 95 were either abortions, miscarriages, stillbirths or deaths from syphilis after birth—a waste percentage of 37.55.

This tremendous waste is due to the presence of the spirochete unhampered by treatment, and it should be most embarrassing to the profession if I were to tell the tales of inadequate treatment and

ignorance in diagnosis which many of the mothers told me. Even in those women who had children with evidence of lues, either no diagnosis was made or no treatment was given. The history of abortions, miscarriages or stillbirths should always make one suspicious of syphilis at once, even in the face of denial by the parents. Diagnosed and properly treated syphilis in the mothers will result in healthy children as we had several opportunities to see—three of the mothers taking treatment during their pregnancies and having healthy children who, up to the present, have negative Wassermann reactions.

Many of the 158 living children had positive evidence of lues while many more had positive Wassermanns without showing any external evidence of the disease.

Some of the congenital lesions were iritis and keratitis, deep gummatous ulcerations in various parts of the body, destruction of the nasopharyngeal tissues, periostitis, Hutchinson teeth, poor physical and mental development. No case had complete blindness and all who have been put under treatment have shown improvements in varying degrees, although it is extremely difficult to alter the Wassermann reading.

Even those apparently normal children, if untreated, may develop symptoms at puberty or as the indirect result of some intercurrent disease, as we had occasion to see in an eleven-year-old girl who had received local treatment for "catarrh of the nose" for one year, at the end of which time the nasal septum and bones together with the soft palate had been completely destroyed. Since taking treatment the progress of the disease has been arrested and she has gained remarkably.

While many children had positive blood findings without external symptoms, in only one case was the converse true, a thirteen-year-old boy who was backward mentally and physically, negative Wassermann, but whose mother was luetic and whose sister was under treatment at Ann Arbor.

In three families, as stated above, sterility was the result probably of the syphilis, and it is not uncommon to find that nature halts the continuation of the disease by preventing pregnancies. A few of the families had many pregnancies—one with 12, 8 living and 4 dead; one with 10, 4 living, 6 dead; 12 pregnancies in another, 7

living, 5 dead; 11 pregnancies, 10 living, 1 dead; a colored family with 11 pregnancies, 6 living, 5 dead.

The history of two families is worthy of notice in detail—Family B.—Grandmother luetic, mother has a four-plus Wassermann without symptoms, father luetic (acquired), one boy with positive Wassermann, hydrocephalus, Hutchinson teeth and poor mentality; baby with no symptoms and a negative Wassermann.

Family E. Grandmother had 10 pregnancies, with 6 deaths, mother claims to have been infected extragenitally and has had 8 pregnancies with 5 deaths, the living children either having luetic symptoms or a positive Wassermann.

At first glance these children appeared to be syphilitic in the third generation, but the history of the fathers and mothers would disprove this. In no case, could we definitely conclude that the infection had been inherited from the grandparents.

In only 47 cases could we obtain Wassermann tests on children, of whom 32 were positive and 15 were negative.

Compared with the statistics published a year ago by Veeder in the American Journal of the Medical Sciences, we have a lower death rate, 37.55% to 55%, his report showing 331 pregnancies in 100 families, 149 living children, 182 deaths.

Is there any reason for the appalling prevalence and spread of syphilis? We believe that *ignorance* is responsible for more cases of luetic infection than any other single factor. Ignorance not only of the disease itself and its symptoms, but also of the various ways in which contagion may occur and methods of prophylaxis. How many parents instruct their adolescent children in the dangers of venereal disease and how many are there who are qualified to impart this knowledge? Such parents are the exception, the vast majority of them being restrained by a feeling of false prudery from warning their children. It is rare for young adults to receive instruction from a family physician with regard to his (or her) sexual life, and he is the one qualified and most fitted to impart that knowledge. Even as children, we are warned against other contagious diseases which are of less consequence than syphilis, yet no warning of syphilis is conveyed to the young adult who is then left to acquire his knowledge by bitter experience. Among girls it is the exception to find any who have ever heard of syphilis before being initiated into a sexual life,

and even among men, their previous knowledge was most hazy and indefinite—far too little to enable them to take any precautions.

This state of affairs could be remedied, in part at least, by widespread instruction of the younger generation by common sense talks, recognizing the fact that sexual development is a law of nature in the growing child and that sooner or later the instinct will demand satisfaction whether the individual is aware of the dangers or not. This attitude may be objected to by some as tending to induce sexual thoughts, but it should be far better to run the chance of that contingency in a few, than to deny to many the knowledge that will enable them to prevent contagion. This instruction should include the various methods in which syphilis is spread in an innocent manner as well as the sexual. Explicit instructions should always be given individuals in an active luetic state, and in the case of prostitutes or those who would be a city charge, compulsory hospitalization should be enforced for at least as long a time as the infected person has open lesions. Those cases should be followed up after discharge from the hospital as is being done at present at Harper Hospital by the Social Service Department and patients should be urged to complete the cure by continued treatment even though all signs of an active syphilis have ceased. They should also be informed of the danger of developing tabes or paresis if treatment is neglected, and the percentage of syphilitic cases at Pontiac should be incentive enough for anyone.

Since talking with some patients who have traveled extensively all over the world, I am convinced that the segregation of prostitutes, properly enforced, is the best method of dealing with a necessary evil. If carried out efficiently with a frequent and rigid examination it should do much to reduce the spread of syphilis. Unless the measures are thorough, visitors will have a false sense of security and would take fewer sanitary precautions than otherwise.

If necessary to check the spread of syphilis a protective application could be supplied to those who must worship at the Shrine of Venus, although a thorough ablution with plenty of soap and water should be sufficient, as it has recently been shown that ordinary soap will easily kill the spirochete. The use of prophylactic measures in the army and navy has proved of great value, but the clergy and the women would raise a storm of protest if means to prevent venereal

disease were placed in the hands of young men. Man is immoral anyway, so why not add to the health of the race by prevention rather than by trying to restrain natural impulses? It is better for a few to suffer than for all.

Prohibition should have an influence to a greater or less degree upon the spread of syphilis, but it should be national and not merely local.

In taking means to control the spread of syphilis, the fact should be recognized that it has an ineradicable instinct as a cause for its existence and that it can not be stamped out as it is possible to do with other diseases. If the sexual instinct could be abolished, syphilis could be likewise, but as the perpetuation of the human race is dependent upon that instinct, so will syphilis exist as long as man does. The most hopeful view appears to me to be education of the young, prophylactic measures that actually protect and the enforcement of the new law regarding detention and treatment of those who, by reason of their calling, are in a position to infect many men—and through them the wives and future generations.

I am greatly indebted to the Social Service Department of Harper Hospital for their invaluable services and also to Dr. Morse and Dr. Crump with their assistants of the Pathological Department for their kindness in making many Wassermann tests.



## ON SALVARSAN ICTERUS

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IT has been observed by Ehrlich and by others that in certain instances the administration of salvarsan is followed by untoward symptoms which may at times be very severe and even terminate fatally. Wechsleman and others doubted the toxicity of salvarsan, and gave different explanations for the salvarsan disturbances. Some ascribed it to faulty technic, others to flooding of the tissues with the proteins of the destroyed parasites; others such as Kerl state that they are due to a "substandard constitution," and especially to a weakness on the part of the lymphatic and vascular systems. Kerl, for instance cites the example of two brothers who, having contracted syphilis, succumbed to salvarsan treatment, exhibiting similar symptoms.

In line with Kerl's hypothesis we may mention Fischer's analysis of the mortality of salvarsan administration in which he shows that in many instances, coincident mercurial poisoning or unsuspected complications of syphilis, such as tuberculosis and pneumonia were responsible for the fatality and concludes that evidence to date exonerates salvarsan from all the serious mishaps that have been accredited to it. He goes so far as to assert that "the cases which justify the assumption that toxic symptoms followed salvarsan injection have been imperfectly investigated."

Of course, there is no reason why, occasionally, after injection of salvarsan severe symptoms may not arise that have no direct bearing on the arsenic injection.

Severin and Heinrichsdorff for instance report two cases that gave after salvarsan marked clinical evidence of hepatic disease simulating acute atrophy before death and at the autopsy showed evidence of marked degenerative changes in the liver. The ques-

tion was raised whether the liver changes were induced by the arsenic or were the results of syphilis. They came to the conclusion on the autopsy findings that the degenerative changes in the liver in one case were due to the arsenic and in the other were probably due to endotoxins derived from the spirochete pallida.

The toxic effects of salvarsan may be very slight or extremely grave. Wilcox and Webster in their study of the toxicology of salvarsan found that in the great majority of cases only slight symptoms follow, and comprise nausea, vomiting, slight rise in temperature (occasionally a high temperature), slight headache and mild diarrhea. The more severe symptoms are of two types. The first type is that of profound toxemia. They appear usually within three days of the injection and comprise collapse, mental disturbances, stupor, muscular twitchings, pain in the abdomen and back, scanty urine with albumin and casts, epileptiform convulsions, coma and death. In this type the liver, heart and kidneys show degenerative changes which account for the profound autointoxication similar to uremia. The second type is that of arsenical poisoning proper and includes rigor, headache, pains in the extremities, nausea, vomiting, furred tongue, diarrhea, injected conjunctiva, erythema, jaundice and occasionally delirium followed by stupor, and albumin and casts in the urine.

Professor Theodore C. Janeway, in discussing Brown's paper, cited below, gives the symptoms of salvarsan poisoning in a case under his care as follows: ". . . Hindoo who, as the result of an apparently safe dose of salvarsan, developed the most intense renal lesion, with blood in the urine, marked oliguria, edema, and in addition jaundice, with a swollen liver, which still persisted when he left the hospital in fair convalescence at the end of nearly two months. At one time, I feared he was going to have acute yellow atrophy of the liver. He evidently had extensive necrosis within the liver. . . ."

We are interested in this paper, especially with salvarsan ieterus, and in this connection a recent article by W. H. Brown, in which he gives an excellent report of liver lesions produced by arsenicals may be profitably cited. He and Pierce injected a number of organic arsenical compounds, synthesized by Jacobs and Heidelberger, into a series of animals—rats, mice, guinea pigs, etc., and ob-

served that the different arsenical compounds produced varying lesions in the different organs of the body. He classifies them into three groups:

1. The *diffuse* lesions which show no preference for any particular region or structure of the lobule. They may be general or focal, and may appear in a widely distributed necrosis of individual liver cells.

2. Lesions of the *central zone* of lobules which include degenerative processes and necroses. In some instances fatty degeneration of the central zone of the liver lobule is the most constant and striking lesion. In other instances, fatty degeneration gives place to necrosis, and most of these central necroses differ in no wise from the central zone necrosis produced by a large number of other chemical agents.

3. The lesions found in the structures of the *portal space* and the *periphery* of the lobule. In large arsenical doses complete necrosis is found of all structures in the portal space and of the surrounding zone of liver cells. In smaller doses the structures which manifest the greatest degree of injury are the bile ducts, while there is only a slight degree of fatty degeneration of the peripheral liver cells.

#### REPORT OF A CASE

About six months ago a patient, presenting the following history, came for relief of his symptoms:

X. Y., white man, age thirty-five years, married, and has one child.

*Past History.*—When one and one-half years old had diphtheria. Has had no other diseases of childhood.

*Veneral History.*—Has had several attacks of gonorrhea. Denies syphilis. There is, however, a possible history of parental syphilis. (The Wassermann of parents was negative.)

*Present History.*—In order to make certain that no syphilis was present in the patient his physician had his blood examined for the Wassermann test with positive findings. His physician thereupon recommended several injections of salvarsan.

About seven days after the first administration of salvarsan (0.4 gm.) the patient after a champagne supper felt bad in his stomach and vomited twice. At one P.M. of the following day he received the second dose of 0.4 gm. salvarsan. At two o'clock he had a good dinner, which was followed by a severe chill (at two-thirty P.M.) and a high temperature. At eight-thirty P.M. he had another chill, accompanied by aches and pains in his legs, constipation and eye pains.

Accompanying the rising temperature there was noticed severe headaches,

suppression of urine and photophobia. On the third day a rash appeared, and on the fifth day a "patch" of dullness was discovered in the posterior portion of the upper lobe of the lung. The "patch" cleared up rapidly. Temperature persisted for ten days. He had a cough and a "rusty" sputum three days before the "patch" was found. The most severe symptom was jaundice accompanied by pruritus. When he was admitted to the hospital, the jaundice had lasted for about ten weeks, was quite marked and seemed to remain constant. In the ten weeks' time the patient lost about thirty pounds in weight but claimed to have lost no strength. The chief symptoms besides the jaundice were pains in his eyes, digestive disturbances, and nightmares.

*Physical Examination.*—A man of about thirty-five years; complexion muddy gray. Jaundice of eyes and skin, some emaciation. The heart and lungs are normal, the liver is somewhat enlarged, smooth with round edges. Pain and tenderness over the region of the gall-bladder. The spleen is not enlarged, the abdomen is relaxed and soft.

*Laboratory Examinations.*—The urine analyses: At the onset of the illness, patient had a trace of albumin, bile, indican, a few granular casts, a moderate number of pus cells, and an occasional erythrocyte. After a few days' time the casts disappeared but the white blood cells, albumin, and bile persisted. The blood count did not show any infective process. R.B.C. 3,800,000. W.B.C. 6,100, polynuclear neutrophils 57%, small mononuclear 34%, large mononuclear 5%, transitional 1%, eosinophiles 3%, hemoglobin 85% (Sahli), viscosity 5.2, coagulation time eight minutes.

*Eyes.*—(Report of Dr. Whithaut of Johns Hopkins)—The right eye showed an old organized retinal exudate or hemorrhage, possibly an incipient partial atrophy (not necessarily specific).

He stayed at the hospital ten days. During this time his temperature ran between 97° in the morning, and 98° in the evening—his pulse between 50 in the morning and 60 in the evening. His digestion somewhat improved. His urinary secretion was good and bowels moved freely when on general diet, but became constipated when he was on fat-free diet. His eye pain and headache disappeared, his weight increased to 146 pounds. He slept well, and during the day attended, in bed, to matters of business without fatigue. When he left the hospital March 3, he was still deeply jaundiced. April 17, 1916, he had only a slight general shade of jaundice, except a darker jaundiced oval area two and one-half inches wide and nine and one-half inches long on the right side of his back extending from his vertebral column to within two inches of the umbilicus. The patch was darker in the back than in the front. At this time his general appearance was good, and in spite of hard work at his business, he has regained his usual weight of 162 pounds. His urine showed no bile although his liver was still somewhat tender. June 17, 1916: No visible jaundice. The dark area was about one-half inch smaller in its width and length and its color lighter. He was feeling well, and his weight was up to 165 pounds. The liver was found still slightly tender. October 16, 1916: perfectly well. No liver tenderness could be elicited. At our request the patient's eyes were now examined by Dr. A. Krebs, February 2, 1917. "The fundi were found normal, muscle balance normal, media clear. The pupils, however, show slight deviation from normal, the right

slightly larger than the left. The reaction to light a little sluggish, otherwise good."

The Wassermann test was performed several times with negative results. Whether the positive test previously reported had been erroneous observations, or whether the salvarsan therapy had caused the negative results is a question which of course can not be decided. The last Wassermann taken Dec. 20, 1916, about a year since the onset of illness was found still negative, although the patient has had no specific treatments.

It was thought advisable to determine whether or not the obstruction to the flow of bile was also causing obstruction to the flow of pancreatic juice. Accordingly the following examinations were made:

## STUDY OF URINE

- March 10. Routine urinalysis, trace of albumin, moderate number of white blood cells, few red blood cells, few hyaline and granular casts. Bile and moderate amount of indican. Arsenic in urine negative. Lactic acid in urine negative.
- " 8. Wohlgemuth Noguchi test on freshly voided urine showed presence of amylase (pancreatic insufficiency).
- " 9. *Salkowski-Kojo* for colloidal nitrogenous substance was positive.
- " 9. *Salomon-Saxl* test for "neutral sulfur" was negative.
- " 13. *Biliary findings in urine*: Bilirubin, urochrome and urochromogen positive. Urobilin, urobilinogen and uroerythrin negative.
- " 17. Urobilin absent. Bile pigment greatly reduced.
- " 19. Bile in urine diminishing in quantity. Urobilin marked.
- " 18. Urobilin present by spectroscope, Ammoniacal Zinc Chloride test.
- " 21. Bile trace, Urobilin present, Gerhardt, Wirsung and ether-absolute alcohol tests.
- " 23. Bile present.
- " 24. Bile trace; March 27, no bile by Gmelin or Nakayama tests.
- " 28. Faint trace of bile.
- " 10. Urine normal.

## STUDY OF INTESTINAL CONTENTS

- March 9. Analysis of Duodenal Contents—Bile, none; Trypsin, good (Gross' Method). Amylopsin (Wohlgemuth Method) fair. Steapsin (as tested by milk) good; Bile, negative.
- " 31. Analysis of Feces—No bile, no pigments, no salts or acids.
- " 9. No pigments, no acids. Test made seven times and found negative by the Schmidt, Steensma, Rosenbach, Huppert, Hammersten, Bonanno, Pettenkofer, Mylius, von Udransky and Neukomm's tests.
- " 10. Analysis of feces for amylopsin and trypsin gave positive results. fat moderate.
- " 11. Bile, doubtful (Schmidt).
- " 12. Digestion of protein and carbohydrate good, fat poor.
- " 13. Analysis for arsenic, negative.

- March 16. Analysis of feces for nitrogen, carbohydrates and fat, after Schmidt-Strassburger diet, marked off by Carmine, showed nitrogen and carbohydrates digestion not interfered with, but a greatly increased amount of fat was found.
- “ 17. Digestion good, trace of bile present.
- “ 11. Fine trace of bile in feces by bichloride method and by Steensma method.
- “ 16. Schmidt-Strassburger test: Protein and carbohydrates normal, fat greatly reduced.
- “ 18. Bile present by Steensma and Schmidt tests.
- “ 19. Bile increased, urobilin and urobilinogen.
- “ 21. Bile present.
- “ 22. “ “
- “ 23. “ “
- “ 28. Bile present in increased amount.

#### DISCUSSION

While at the West Penn Hospital his illness was diagnosed as salvarsan poisoning.

The disturbances caused by the salvarsan followed about one hour after the injection in a man that had always enjoyed excellent health, never had any symptoms of syphilis, and denied ever having contracted it. While it is true that a specimen of blood examined by three men showed two-plus before the salvarsan injections, the five Wassermanns taken, the last two years after the injection of salvarsan, were all found negative. Kerl's and Fischer's theories about the toxic symptoms being due either to a substandard constitution or to manifestations of syphilis itself can not apply to the case under discussion. Even if the acute gastric irritation present in the patient prior to the treatment be sufficient to place him in the category of the "substandard constitution," the salvarsan must be admitted to have been the cause of the illness.

The symptoms that followed the injection correspond to those of the type of salvarsan poisoning cited above, described by Wilcox and Webster as symptoms of "arsenical poisoning proper."

Our patient had in a severe degree the rigor, the headache, the pain in the extremities, the nausea, vomiting, jaundice, erythema, eye and kidney disturbances that are described in that type.

Of course, there was no way of confirming the diagnosis by tissue examination, the patient having recovered, but the laboratory

studies cited above gave us, to a very satisfactory degree, the assistance needed in the confirmation.

No bile at all has passed through the common duct into the bowels, as evidenced by the duodenal tube and the repeated examination of feces. The pancreatic secretions found entrance into the duodenum as was proved by the duodenal tube, the Schmidt-Strassburger and the Wohlgemuth tests.

There was never found glycosuria, and no pancreatic tumor was ever palpable.

Now the icterus must have been due either to interference of the passage through the ducts into the bowels of bile normally formed in the liver, or to the interference with the formation of bile. If the first was the correct explanation, there must have been either a complete obstruction or obliteration of the common duct, the pancreatic secretions passing through an independent opening, or the lower part of the duct must not have been involved in the obstruction or obliteration.

As this disease came on acutely in the patient who had enjoyed excellent digestion before, we could exclude obliterated common duct and assume an obstruction in common duct by stone or pressure of a diseased pancreas (inflammation or tumor), or by catarrhal jaundice.

We excluded stone in the common duct (1) by the history, by the absence of pain in that region, by the symptoms of acute illness of ten days' duration that had no bearing on biliary tract. (2) By the persistent complete absence of bile in feces for about three months unaccompanied by pain, too tight and painless obstruction for a stone. We excluded pancreatic pressure by the perfect pancreatic functions, the free admission to duodenum of its secretion and by the absence of a mass in the pancreatic region.

We excluded catarrhal jaundice although it seemed plausible because the patient vomited before the salvarsan was given and the digestive disturbance that started before the injection of salvarsan might have extended to the duodenum and common duct causing thickening of their mucous membrane and swelling of the glands at the diverticulum of Vater (Eppinger). But the early course of the disease, the involvement of kidneys, eyes, chest, skin and the absence of gastrointestinal disturbance the first three days do not

correspond with the picture of catarrhal jaundice. Weil's disease or infectious jaundice might have been considered with more justification if the icterus had not lasted so long.

Syphilis of the liver was excluded by absence of syphilitic symptoms in the past, by the good condition of the patient prior to the syphilitic treatment, and by the behavior of the disease after the treatment, by the negative Wassermanns repeatedly taken, the last one about a year after onset of disease. One might suggest the possibility of latent syphilis called into activity by provocative treatment with salvarsan. But in the first place it is very doubtful whether two doses of 0.4 of salvarsan is a sufficient provocative treatment for latent or hereditary symptomless syphilis, and, in the second place these two doses can hardly be sufficiently effective as to bring about repeatedly negative Wassermanns for two years. Again the symptoms of this case are not those of secondary syphilis which one would expect to follow a provocative treatment.



## THE TOXICITY OF VARIOUS PREPARATIONS OF ARSPHENAMINE\*

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AT the outbreak of the world war the original German-made "salvarsan" practically ceased being marketed in America as well as in France and England. The demand for this drug had already assumed massive proportions. The natural result of this unsupplied demand was the manufacture of similar, if not identical, products by various other concerns. The Canadian preparation "Diarsenol" and the Philadelphia preparation "Arsenobenzol" were soon marketed in quantities in this country. The French product "Arsenobenzol 'Billon'" has been used less generally in America I believe. Very recently "Salvarsan" has again been put on the market by representatives of the Farbwerke-Hoechst Company who have established laboratories in New York City.

In the recent literature there have been occasional reports of extremely toxic, and sometimes fatal, reactions following the infusion of some of these preparations. That there is ample room for the occurrence of toxic impurities in arspenamine is perfectly apparent when it is considered that dozens of operations are necessary in its manufacture and that the finished product can not be re-purified by recrystallization.

Advantage has been taken of the large syphilitic clinic at The Marquette University School of Medicine in an attempt to arrive at some definite conclusions regarding the relative toxicity of these preparations of arspenamine. An attempt has also been made to draw some conclusions regarding the various factors responsible for the reactions which so frequently follow the administration of the drug. That the comparison between these various preparations

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might be the more accurate, identically the same technic was used in all cases reviewed as a basis for this article.

The toxic reactions resulting from the administration of arsphenamine differ greatly in the time of appearance and in the character of their symptoms. A close scrutiny of these reactions, however, permit them of classification into four distinct types.

The *gastrointestinal* reactions are by far the most commonly seen. This type of reaction develops from one-half to six hours after administration of the drug and commonly lasts three to twenty-four hours. Nausea, vomiting, and a chilly sensation (or possibly well developed chills) mark its onset. A stubborn headache soon develops and frequently persists for one or two days. In the more severe reactions of this type a moderate fever with profuse sweating sometimes occurs. The early symptoms usually subside within four to six hours after which a diarrhea develops and persists for one or two days. This type of reaction is never fatal.

The *vasoparetic* reactions are less common but much more severe than are those of the gastrointestinal type. This type of reaction develops during or immediately after administration of the drug and seldom lasts over thirty minutes, although it is commonly followed by a typical gastrointestinal reaction. As the name implies, the vasoparetic reaction is symptomatized by evidences of a paralysis of the vasoconstrictor mechanism. The patient feels faint, full-headed, and dizzy. The face becomes flushed, cyanotic and finally very pale. The lips and eyelids sometimes become puffed and edematous. There is slight dyspnea and the patient hungers for air. The pulse is at first full and bounding; later rapid and thin. As the vasomotor paralysis wears off vomiting and rigor develop and the patient continues in a typical gastrointestinal reaction. Although patients suffering a vasoparetic reaction appear *in extremis* for a few moments, recovery is usually prompt and complete.

The *cerebral* reactions are fortunately very rare. This type of reaction usually develops two or three days after administration of the drug and frequently terminates fatally. The symptoms are cerebral. The reaction begins with headache and projectile vomiting. A moderately high fever continues. Epileptiform convulsions

usually occur. The reflexes are at first exaggerated but finally lost. The reaction terminates in coma and death.

The *epidermal* reactions are also very rare. This type of reaction develops from two hours to several days after administration of the drug and varies as much in its length. The chief manifestation is that of an eruption, usually scarlatinoid or urticarial in character. A severe jaundice has been observed to follow the infusion of arspenamine. Such a jaundice usually appears late and frequently terminates fatally with the symptoms of acute yellow atrophy of the liver.

A multitude of factors have been proposed to explain the occurrence of reactions following the administration of arspenamine. All of these proposed factors fall under three great headings: those pertaining to the composition of the drug; those pertaining to the technic employed in its administration; and those pertaining to the individuality of the patient. It is very probable that all of these factors have some bearing upon the toxic reactions following the infusion of arspenamine. It is likewise very probable that the relative significance of these three factors varies a great deal in different individuals and in the same individual at different times.

No one would dispute that the technic employed in the infusion of arspenamine has a great influence upon some reactions following its administration. The alarming and frequently fatal reaction following the use of an acid solution of the drug is, in itself, sufficient to demonstrate the importance of this factor. It is a great question, however, whether the slight variations between the common methods of administration of arspenamine really have any bearing on the reaction following. It is generally conceded that the solution should be alkalized, that it should be sterile, that it should be about body temperature, and that it should be administered slowly. It is also conceded that the solvent water should be freshly distilled. This is, of course, good scientific practice, but I have purposely used water as old as two days in a series of cases without noting any increased toxic effect.

There is one radical difference in the technic of administration of arspenamine upon which no conclusive comment has occurred. Many physicians prefer the use of a weak saline solution of the

drug, whereas many other physicians prefer the use of a concentrated aqueous solution. Purely as a matter of economy of time, the concentrated aqueous method (0.4 gm. to 50 c.c. water) has been employed routinely at the dispensary. If those with whom I have talked have taken pains to inquire minutely into the reactions experienced by their patients it would seem that I have had slightly more reactions of the gastrointestinal type as the result of using the concentrated aqueous solution.

It has been pointed out that a solution of arsphenamine deteriorates rapidly. All are familiar with the dark color which the solution acquires on standing. Little comment, however, has occurred on the rapidity with which a prepared and alkalized solution of arsphenamine becomes toxic. It has been the custom at the dispensary to prepare and alkalize as many as six doses of the drug at one time rather than make each dose separately. This has been done repeatedly, and a close scrutiny of the reactions has failed to furnish any evidence that the sixth patient, whose solution was prepared thirty minutes before, suffered any more reaction than the first patient, whose solution was prepared freshly.

So much for the bearing which the technic of administration has upon the reaction following the infusion of arsphenamine. Withal, I am inclined to the belief that so long as the proper consideration has been given the principles of dosage, asepsis, alkalization, and the use of pure water and sodium hydrate, the minor variations in the technic of administration of the drug have little, if any bearing upon the resulting reaction.

Those factors pertaining to the individuality of the patient seem to have more bearing upon arsphenamine reactions. This is particularly true in regard to the gastrointestinal type of reaction. I have records of several patients who, with an ordinary dose of any of the preparations of arsphenamine, persisted in having a gastrointestinal reaction. I have records of several other patients who failed to experience a reaction after receiving an ordinary dose of any of the preparations of arsphenamine. It would seem that the former were particularly susceptible to, and the latter particularly refractory to, gastrointestinal reactions. As a general rule, women suffer stronger reactions than men. Children between one and ten

years of age bear their proportionate dosage of arsphenamine with distinctly less discomfort than do adults.

The question of the preparation and after-treatment of a patient receiving arsphenamine seems to be of some importance in connection with the gastrointestinal type of reaction. It has seemed to me that those patients having a preliminary cathartic suffered more gastrointestinal reactions than those who had neglected it. The fact that the patient has eaten an ordinary meal two or three hours before treatment seems to have no effect on the resulting reaction. The question of eating after the injection, however, has a very definite effect upon the reaction. A number of patients have volunteered the information that they remained perfectly well after their treatment until they ate a hearty dinner or supper, whereupon they became nauseated and vomited. In reviewing the factor of individuality, it seems that some patients are particularly refractory to, and others particularly susceptible to the gastrointestinal type of reaction and that the eating of a heavy meal within six or eight hours after treatment definitely increases the degree of gastrointestinal reaction.

The third and by far the most potent factor influencing the reaction following the infusion of arsphenamine is that of the toxicity of the drug itself. My experience would not warrant any conclusion as to the factor responsible for the cerebral and the epidermal types of reaction. It has been a basis, however, for some very interesting deductions regarding the vasoparetic and gastrointestinal types of reaction.

It has been pointed out **that the** factor of individuality has some bearing upon the gastrointestinal reactions resulting from arsphenamine injections. It has been observed, however, that with the same patient, the same dosage, and the same technic of administration, stronger reactions were invoked by one preparation of arsphenamine than by another. Pt. No. 4275 suffered a strong gastrointestinal reaction after each of two doses of 0.4 gm. diarsenol but received 0.4 gm. arsenobenzol without reaction. It has been observed that one preparation of arsphenamine given to a group of patients resulted in distinctly more and stronger reactions than another preparation given in the same size dose and with the same technic to another group of patients. On Feb. 8 a dose of 0.4 gm.

"diarsenol" was given to each of nine adults. There resulted two strong and four moderate gastrointestinal reactions. Three escaped reaction. On Feb. 28 a dose of 0.4 gm. arsenobenzol was given to eleven adults without the least reaction. The technic was identical in both instances. It has also been observed that one control lot of a preparation of arsphenamine provoked more reactions than another control lot of the same preparation. A dose of 0.4 gm. arsenobenzol, lot No. 525, was given to each of four patients. There resulted one strong and three moderate gastrointestinal reactions. With precisely the same technic throughout, 0.4 gm. of lot No. 1030 arsenobenzol was given to eight patients without the least reaction. Such experiences seem to warrant the conclusion that there is something in the drug itself that is responsible for at least a part of the gastrointestinal reactions following the administration of arsphenamine.

That the drug is entirely responsible for the occurrence of the vasoparetic reactions seems beyond question. In an earlier article<sup>1</sup> I reported three vasoparetic reactions resulting from the administration of a batch (lot BDB) of the new American-made salvarsan to five patients. The mere fact that but one similar reaction resulted from the administration of some two hundred doses of other preparations of arsphenamine seems to prove conclusively that those three reactions were produced by some toxic element in the salvarsan itself. This is even more apparent when it is considered that the technic of administration has been uniform throughout and that those three patients have received several injections, either before or since, of even larger doses of other preparations of arsphenamine without the least reaction.

In support of this contention we have no less an authority than Schamberg<sup>2</sup> stating that a toxic by-product sometimes develops during the process of manufacture of arsphenamine which has so far defied recognition, but which is known to exert a very strong vasoparetic action. It is interesting to note in this connection that the injection of arsphenamine into laboratory animals offers no valuable control of this vasoparetic by-product because the animals either survive or die, never exhibiting the typical reactive phenomena seen in the human<sup>2</sup>. Whatever this vasoparetic element may be, it is certain that it is very highly potent. Pt. No. 4904 developed

an alarming vasoparetic reaction before he had received 0.2 gm. of the new salvarsan.

In compiling the comparative results obtained by the administration of the different preparations of arspenamine all cases were excluded in which more than 0.6 gm. or less than 0.3 gm. of the drug was used because patients receiving more than 0.6 gm. of any of the preparations seldom escaped reaction, whereas no reaction was noted in those receiving less than 0.3 gm. of any of the preparations. The French preparation "Arsenobenzol 'Billon'" was used in but a limited number of cases because of the expense and difficulty with which it was procured. The use of the new salvarsan ceased after the first batch of five doses because of its apparent extreme toxicity.

Of 77 doses of "diarsenol," there resulted thirty-five per cent gastrointestinal reactions and one and one-half per cent vasoparetic reactions.

Of 97 doses of "arsenobenzol," there resulted five per cent gastrointestinal reactions and no vasoparetic reactions.

Of 19 doses of "arsenobenzol 'Billon'" there resulted twenty-five per cent gastrointestinal reactions and no vasoparetic reactions.

Of 5 doses of the new "salvarsan," there resulted sixty per cent vasoparetic reactions.

#### CONCLUSIONS

1. Gastrointestinal reactions resulting from the administration of arspenamine are largely the result of impurities in the drug.

2. Vasoparetic reactions resulting from the administration of arspenamine are entirely the result of impurities in the drug.

3. Of the four preparations of arspenamine commonly used in this country, the Philadelphia preparation "Arsenobenzol" has the preference by being distinctly the least toxic.

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## ON THE USE OF AMERICAN-MADE SALVARSAN

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THE manufacture of salvarsan in this country is one of the most hopeful signs in modern pharmacology. The manufacturing chemists of America have shown remarkable aptitude since the beginning of the war in reproducing chemicals of foreign make. Salvarsan, on account of the complexity of its manufacture, has been exceedingly difficult to reproduce, but that this has been successfully accomplished is manifested by the production of this arsenical preparation under the trademark name of salvarsan by the H. A. Metz Laboratories. Since August, 1917, I have given over five hundred injections of American-made salvarsan and I can see no difference between it and the imported product. The drug goes into solution as rapidly as its foreign prototype and the clinical and serological results are quite as good as those following the use of the older product.

Four cases, which came under observation soon after the initial appearance of the lesion, may be taken as an example of the effectiveness of the domestic salvarsan. Diagnosis was confirmed by the demonstration of the *Treponema pallidum* by dark-field illumination. All Wassermanns were negative.

In each instance the patient was given an initial dose of 0.3 gram. As it was well borne the second dose, seven days later, was increased to 0.4 gram, without any sequelæ. The chancres rapidly disappeared. Subsequent doses were 0.6 in three patients. The fourth became sensitized after the seventh injection and the remaining injections, three in number, were 0.3.

The dilution was at first 20 c.c. sterilized freshly distilled water to the decigram of salvarsan. At one injection period the dilution



was lowered to 10 c.c. per decigram. This concentration was followed by a considerable reaction in one case and moderate reaction in two others.

A week later these patients were given the same dosage from the same batch from the laboratory diluted to 25 c.c. to the decigram and the injections were accomplished absolutely without incident and, although each person received several subsequent treatments with the less concentrated solutions, no reactions were noted.

This emphasizes the advisability of carrying out Prof. Ehrlich's strict admonition regarding the heavy dilution of salvarsan solutions.

These four patients had from six to nine injections at weekly intervals, with mercury every seven days. Two were given hypodermic injections of one grain each of hydrargyri salicylas in liquid albolene and another hydrargyri succinimide in a neutral base with anesthesin, while the fourth used the succinimide every other day as an inunction.

In the four cases in question the blood still remains negative, no secondaries have appeared, and there were no demonstrable symptoms of the disease after the provocative salvarsan.

In addition to the cases in question many injections were given to other patients already under salvarsan treatment. The use of the older product was followed by the American product without incident.

There are certain points which come to mind which warrant particular emphasis. The principal one is that of reactions. All users of salvarsan have had reactions of greater or less severity in times past, and many medical men fear to use a powerful product like salvarsan if they get a few reactions. Without any doubt, there are numerous causes for reactions.

Wassermann blames the bacterial proteins in the water: Wechsellmann, the rapid dissolution of great quantities of spirochetes and the freeing of their constituent parts. Some ascribe it to the "setting free of some toxic substances from the spirochete," or to the "liberation of endotoxins from the killed organisms," or to "imperfections in the physician's technic," while still others to impurities in the drug itself.

Without doubt, each reason is tenable and reactions might be

caused even by two of the reasons ascribed acting simultaneously. I am convinced, however, after a large experience in the administration of salvarsan that the febrile and gastrointestinal disturbances which may follow the injection will be found due to one or more of these causes:

1. Concentration of solution.
2. Presence of partially digested food in the gastrointestinal tract.
3. Imperfect cleansing of the alimentary canal.
4. The use of impure sodium hydroxide.
5. The use of imperfectly sterilized absorbent cotton.
6. The use of old distilled or imperfectly sterilized water.
7. Failure to neutralize the solution, thus injecting an acid solution.

The use of a concentrated solution of salvarsan is inimical to the patient. Four decigrams of salvarsan should be dissolved in not less than 100 c.c. of sterile, freshly distilled water and six decigrams in not less than 150 c.c. and injected slowly. No food should enter the stomach for at least six hours before the injection or for four hours afterward. For that reason it is well to administer the drug in the late afternoon.

The patient should have a complete catharsis the morning of his treatment, so that the intestinal canal may be free from extraneous material.

In preparing an alkaline solution by means of sodium hydroxide, the hydrochloride is converted into the soluble disodium salt of the insoluble base dioxydiamidoarsenobenzene. Before adding the sodium hydroxide it is absolutely essential that every trace of salvarsan should be dissolved. When a few drops of absolutely chemically pure, freshly prepared sodium hydroxide are slowly added, a turbid mixture results, which clears upon the addition of a few more drops. Four drops should be used for each decigram of salvarsan, or 16 for 0.4 and 24 for 0.6 dosage.

The administrator should be absolutely certain that the solution is neutral and he should satisfy himself to this effect by the use of litmus paper or phenolphthalein. Reactions will follow the use of an acid solution and this important matter should not be left to guess work.

Particular emphasis must be placed on the necessity of having the neutralizing agent, sodium hydroxide, not only chemically pure but also made into solution on the day of the administration of the drug. Not long since ten injections of salvarsan were given by the author to patients who had had a varying number of injections. Each patient had a reaction, some moderate and some severe enough to produce purging and vomiting. Indeed, one displayed for a short time symptoms of mental confusion. In view of the care which was exercised in technic, each step of the proceedings was carefully gone over and checked up, and the only conclusion reached was that the sodium hydroxide was at fault. This was sent to a chemist who reported that it contained 13.52 per cent sodium hydroxide instead of 15 per cent and .93 per cent sodium carbonate. While the solution was freshly made, it was learned that the bottle had been utilized for some time for keeping sodium hydroxide, the old being poured out and the new being introduced without washing out the bottle, so that there was a certain amount of decomposed sodium hydroxide in the bottle when each new solution was added. In consequence, this series of reactions occurred. When these patients next returned for an injection, the same control number was given as was used at the time of the reactions, but the sodium hydroxide was freshly prepared. There was no difficulty whatever following the administration of the salvarsan with the fresh neutralizing agent, and since this fault was corrected, no difficulty of this nature has resulted.

One of the most important factors in this technic is the matter of filtering. I have previously called attention to the danger of using sterilized absorbent cotton for this purpose. (*Medical Times*, March, 1917.) Chemical analysis of some cotton revealed the presence of an acid which is distinctly harmful. The acid was due to the formation of either hydrochloric acid from the bleaching salt of lime, to the action of sulphuric acid with which the cotton is treated to neutralize the alkalinity of the bleaching lime, or to the presence of both hydrochloric and sulphuric acids.

By using heavy layers of thoroughly sterilized gauze, all the difficulties which may follow the use of the absorbent cotton are obviated.

Some physicians do not pay sufficient attention to the matter of

the water employed in making the solution. Men have been heard to boast of using ordinary tap water and many do not attempt to use freshly distilled and sterilized water. At one time, I gave fifteen injections of American salvarsan in the clinic of an institution with which I was not familiar. When I reached the hospital, I was informed that everything was ready for the injections. The first patient showed a slight anaphylactoid reaction and nearly every patient had either a slight nausea or some degree of flushing. Upon investigation, I found that the water had not been sterilized at all and had been obtained from outside the institution. To the best of my knowledge, it was not distilled that day. What disturbing factors may have been in the water I do not know, but the fact remains that these patients reacted to the injections with more or less severity. Subsequent injections given in the same institution with a most careful technic, including freshly distilled and sterilized water, showed no reactions and I am convinced that in this instance the water was at fault.

I have never seen a reaction resulting from the use of American-made salvarsan severe enough to necessitate the use of epinephrin and the only ones of consequence have been the series in which the impure sodium hydroxide and the old distilled water were employed.

Despite the fact that many of these injections have been given in an ambulatory clinic to a class of patients composed of the heterogeneous mass of men who are collected in one of the most populous parts of a great city, the injections have been very free from resultant reactions.

Patients are asked, when they present themselves for mercury injection, if they had any ill effects from the previous salvarsan. Occasionally a man has had some headache and, infrequently, he has had nausea or slight vomiting, but these cases have been the exception rather than the rule, and the writer can say in all frankness that in a very large experience in the administration of the arsenical products, he has been quite as well satisfied with the American-made salvarsan as with the original Ehrlich product.

The question of dosage of salvarsan enters more or less largely into the treatment of syphilis. I have used doses of varying degrees and have come to the conclusion that I get quite as good re-

sults by the employment of 0.4 salvarsan, administered from every five to seven days, as I have from 0.6. Salvarsan is a very powerful drug and it seems apparent that there is more strength in the American than in the foreign product. I, at one time, observed a series of cases in which the Ehrlich salvarsan 0.4 was administered and I was particularly pleased with the results. I am strongly inclined to believe that this size is more satisfactory, particularly in clinics where one is not absolutely certain that the patient has an empty gastrointestinal tract, and where he can not be watched with the same care as obtains when the injection is given at the patient's residence or in the hospital. I realize that my opinions are at variance with those of other syphilographers who crowd the system with an arsenical preparation, administering it anywhere from once in five days to once a day. My experience, however, has not demonstrated the advisability of injections more frequent than once in five days unless these patients can be kept in the hospital and under close observation.

It is a belief founded on the results gained in nine months' trial that domestic salvarsan is the equal of the Ehrlich product, if careful attention is paid to the condition of the gastrointestinal tract and if an exceedingly exact technic, including, of course, freshly prepared c.p. sodium hydroxide, freshly distilled and sterilized water, and an absolutely neutral solution is employed.

# INTRAVENOUS INJECTIONS OF SODIUM IODIDE IN MASSIVE DOSES IN OBSTINATE SYPHILIS

## REPORT OF LARYNGEAL CASE RECEIVING 125 MASSIVE DOSES OF IODIDE, 54 SALVARSAN, AND MANY HUNDRED INTRAMUSCULAR MERCURY INJECTIONS

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THE subject of intravenous iodide administration in general is only scantily represented in the literature, and I have been unable to find any mention of this method as used in laryngeal syphilis in particular. The following report is based essentially on original work on a private patient with laryngeal syphilis, which in spite of intensive antisymphilitic treatment over a number of years suddenly developed progressive features, which unless relieved, would infallibly have required tracheotomy. Independently of the work done by other pioneers along this line, I devised a technic of my own for intravenous iodide medication, which led to such excellent results in an unusually refractory case, that the observation is herewith reported in detail for the guidance of interested practitioners. Personally I have been struck with the similarity in technic and results obtained by contemporaneous fellow-workers in this country and abroad. This patient was presented before a meeting of the New York Medical Union, January 22, 1918, and also before the Section of Rhinology and Laryngology of the New York Academy of Medicine, March 27, 1918.

### CASE OF LARYNGEAL SYPHILIS GREATLY IMPROVED BY INTRAVENOUS ADMINISTRATION OF SODIUM IODIDE

The patient, a robust man of twenty-nine years, native of Russian Poland, became infected in the ordinary way at the age of seventeen (his first offence), contracting an initial lesion of the genitals with considerable glandular swelling in the inguinal region. Treatment in

form of mercurial inunctions was promptly instituted and continued for six weeks; all clinical evidence of the disease had then disappeared and the treatment was stopped. After an entirely free interval of five years the patient's voice became hoarse, and he began to suffer from dyspnea on exertion. At this time (seven years ago), he was told by a physician that he had laryngeal syphilis, and during the next two and a half years he received antisyphilitic treatment fairly regularly from several physicians and dispensaries, without material change in his condition.

When the patient came under my personal observation, four and a half years ago, his general condition was below standard, and well-marked hoarseness and dyspnea were present. The Wassermann test was four-plus. Treatment consisted in a number of full doses of salvarsan, at intervals of a week, and considerable improvement was obtained. Full internal antisyphilitic treatment, varying in detail from time to time, was kept up from now on over a period of two years and seven months, but without material added benefit. The general health was not affected at this time, moderate hoarseness and slight dyspnea on great exertion being the only symptoms complained of.

#### LARYNGOSCOPIC EXAMINATION

Moderate swelling and redness of both arytenoids, and of the folds adjacent and extending downward towards the ventricular bands. Swelling more marked on right side than on left (and this difference persisted.) No dysphagia. No evidence of deep ulceration, tuberculosis, or malignant growth, local or elsewhere in the body. Characteristic findings of late syphilis of the larynx, gummatous in type, bilateral in position.

The gumma in this case did not respond readily to antisyphilitic therapy, in fact proved highly resistant, for during this period (two years and seven months), the patient received 30 doses of salvarsan. 0.6 gm. each, intravenously, besides several hundred injections of mercury salicylate, in  $\frac{1}{2}$  to 1 gr. doses suspended in oil, at intervals of three to five days; the obligatory mercury inunctions; mixed treatment by the mouth; many courses of potassium iodide by the mouth, reaching at times several hundred drops daily; one series of about twenty intramuscular injections of sodium cacodylate in full doses. In spite of this intensive treatment, given according to the customary

plan and pushed to the limit of tolerance, with intervals of freedom from all medication, the sign and symptoms of progressive malignant syphilis finally supervened, in May, 1916, nearly two years ago. The patient had several chills, in no way related to salvarsan or mercury treatment; he was slightly feverish, and so weak that he found it difficult to keep at work.

Examination for evidence of intercurrent infection proved negative. Blood examination (for malaria) negative. Urinary examination, negative. Physical examination negative, except for larynx, which on inspection presented large ovoid swellings of the arytenoids overhanging the vocal cords and almost concealing the chink of the glottis. Sleep was interrupted every quarter to half hour by an impending sense of suffocation. Attempts at swallowing ordinary food invariably brought on an attack of dyspnea. At this time the patient found it necessary to stop working on account of progressive ill-health.

This difficult case, with its urgent and alarming features, was considered by me from every viewpoint, and after the situation had been discussed in all its bearings with some of my professional friends, treatment was begun with six tubes of a commercial preparation claimed to contain iodine in suitable combination with several other ingredients. The daily mercury was now changed from the insoluble salicylate in oil to aqueous solution of the bichloride, which in its turn was subsequently replaced by the double salt, sodium-mercuric iodide. Recognizing the advantages of an iodide solution of known composition, containing a single ingredient, I decided to try out the sodium salt as *a priori* more acceptable to the blood, rather than the more commonly used potassium salt. The technic was carefully worked out as an original procedure, without knowledge on my part of similar therapeutic experiments. The patient assisted by ready and eager consent to all measures for his relief. His experience as a hospital orderly covered more than one fatal tracheotomy, and he was naturally anxious to avoid this emergency procedure by all the means available.

Edema of the glottis, as a danger in the course of iodide medication has been pointed out by some observers, such as Lermoyez, and in order not to aggravate the existing symptoms the potassium iodide by mouth was stopped. The omission of the drug did not, however, lessen the swelling, nor did the intravenous administration



of sodium iodide increase it, as would have occurred in a case of iodide edema. Without material benefit the patient received frequent intravenous doses of salvarsan and intramuscular injections of mercuric chloride solutions, in doses of  $\frac{1}{4}$  to  $\frac{1}{2}$  gr. The syphilitic parasites in this case were evidently mercury and arsenic fast.

#### INSTITUTION OF INTRAVENOUS SODIUM IODIDE TREATMENT

June 24, 1916, initial dose of 30 gr. increasing each dose by five grains, up to a maximum of 335 gr. Suitable veins were very hard to find, after a large number of these injections had been applied, and the treatment often had to be interrupted for a few days, until thrombotic veins had again become permeable, or perivascular swelling had subsided. After an interruption, a smaller dose was usually given, about 200 gr. as a rule, rapidly increasing the size of the dose until the treatment had to be stopped for lack of available veins. Iodism was only exceptionally responsible for a temporary suspension of the treatment; its symptoms were those of gastric irritation and essentially mild, in form of regurgitation of small quantities from the stomach. A cutaneous eruption of petechial spots was occasionally noted. In a general way, the treatment was remarkably well borne, in spite of the enormous daily dosage. It is also noteworthy that the patient preferred the intravenous method of administration, as the iodides given in this way, "did not upset the stomach."

During the entire course of iodide treatment, mercury and salvarsan were likewise administered to the limit. However, within a few weeks after starting the intravenous iodide medication, improvement was so obvious that the patient could eat, sleep and work in comparative comfort. Furthermore, his voice considerably improved and this amelioration continued right up to the time when all intravenous iodide injections were stopped for want of veins.

#### WASSERMANN REACTIONS

During the four and a half years covered by this report about ten Wassermann reports were obtained, always from the same laboratory, and were always four-plus, except once about five months ago when a three-plus report was obtained. It is interesting to note that this followed a prolonged series of mercury injections without salvarsan and that several months later, after giving three doses of salvarsan, in quick succession, in addition to the usual routine mercury, the blood reports came back four-plus, suggesting the *phenomenon of the*

*provocative Wassermann*; another interesting thing in connection with these tests was, that the last blood taken (one month ago), was sent to two laboratories,—the usual, and to another well-known worker in this line. The regular one reported four-plus and the other two-plus with cholesterin reinforced antigen. The patient still has symptoms of active syphilis, although enormously improved, and consequently is entitled to a positive Wassermann.

The following data on the administration and effect of mercury and salvarsan in this patient serve to illustrate most graphically the value of combined treatment in the fight against syphilis.

#### SUMMARY OF MERCURY ADMINISTRATION SINCE EXACERBATION

Elapsed number of days.....663  
 Number of injections.....396  
 Form of mercury, either as mercuric chloride or as sodium-mercuric iodide ( $2\text{NaI}\cdot\text{HgI}_2$ ).

Dosage  $\left\{ \begin{array}{l} \text{Minimum, } \frac{1}{8} \text{ gr.} \\ \text{Maximum, } \frac{1}{2} \text{ gr.} \\ \text{Average, } \frac{1}{4} \text{ gr.} \end{array} \right.$

Amount of mercury for the period.....105 gr.  
 Average dose per day for the period (663 days),  $\frac{1}{6}$  gr.

Previous to the exacerbation, mercury was given chiefly in the form of salicylate suspended in oil in doses of  $\frac{1}{2}$  gr. to 1 gr. every three to five days; but after the patient's condition had become worse in spite of treatment it was deemed advisable to use a soluble compound, and the mercuric chloride was chosen and a solution containing one grain of the bichloride to one dram of distilled water was used; but after using this for some weeks I devised the following formula and have used it ever since, as it is less caustic to steel needles; less irritating and consequently less painful to the tissues, and the doses as used are identical in mercury content with the bichloride and equally efficient.

#### Formula:

Mercuric chloride .....	1 gr.	$\left\{ \begin{array}{l} \text{M}\bar{\text{v}} = \frac{1}{12} \text{ gr.} \\ \text{M}\bar{\text{x}} = \frac{1}{6} \text{ gr.} \\ \text{M}\bar{\text{xv}} = \frac{1}{4} \text{ gr.} \\ \text{M}\bar{\text{xxx}} = \frac{1}{2} \text{ gr.} \end{array} \right.$
Sodium iodide .....	3 gr.	
Distilled water up to	60M.	

This forms a perfect solution of the double salt sodium-mercuric iodide ( $2\text{NaI}\cdot\text{HgI}_2$ ).

I find this formula most satisfactory for intensive treatment, but it must be given at intervals of one, two, or three days and when given properly it is less apt to cause salivation than the insoluble compounds which are given less often, but in larger doses. The bichloride is 74 per cent elemental mercury, whereas the salicylate is but 59 per cent mercury.

#### SALVARSAN ADMINISTRATION

*Before Exacerbation:*—From October, 1913, to May 24, 1916, a period of two years, seven months, he received thirty salvarsan injections 0.6 gm. each, averaging one per month, although they were usually given in courses of about three doses at intervals of one each week and then a longer period intervening during which mercury intramuscularly and potassium iodide by mouth were given.

*After Exacerbation:*—From June, 1916, to April, 1918, a period of one year, ten months, a total number of twenty-five salvarsan injections were given with a minimum of 0.6 gm., maximum of 1.2 gm., averaging 0.9 gm. per dose or 1.0 gm. per month. These were also given in groups of three usually and then a period of rest. Following these large doses a fairly severe chill ensued, with headache, vomiting and mild temporary looseness of the bowels. The last two injections given were 1.2 gm. each, one week apart; following the first nothing extraordinary was noted, but after the second a mild acute transient nephritis developed, lasting for a short time and accompanied by albumen casts and renal epithelial cells in the urine and pains across the back; later a few neuritic pains in the legs and slight parasthesias were noted and he was incapacitated from work for two days by the pain across the lumbar regions.

Intramuscular iodide medication probably saved this laryngeal case a tracheotomy and possibly also his life. He still has syphilitic swelling of the arytenoids, but his condition is enormously improved and he suffers no discomfort, although he has not improved much under mouth administration of the iodides since the intravenous treatment had to be discontinued for want of available veins fourteen months ago.

*Other Cases:*—Although this report is primarily based on one specific and especially intractable case, I have also used the iodides in this way in five other patients with nonsyphilitic conditions (chronic

rheumatism and gout). Thirty-two doses of sodium iodide, ten to thirty-five grains each, averaging twenty-one grains; also three doses of potassium iodide, fifteen grains each were given usually combined with sodium salicylate. No ill effects were noted and in two of the cases (one gout and one rheumatic), the conditions cleared up almost like magic. One rheumatic patient was a man of eighty years, who had been rejected for life insurance forty years before on account of a weak heart. At the time of treatment he had chronic interstitial nephritis and had just recovered several months before from an attack of pneumonia; he received some benefit and showed no ill effects from this form of medication.

A very interesting interrelationship exists between mercury and iodides in connection with the production of *chills*, as will be shown by the following section taken from the records:

Up to this point the iodide was given in the veins—mercury in the muscles.

Aug. 14, 1916—155 gr. Na I	c̄	Hg Cl <sub>2</sub>	1/6 gr. intravenously—No chill
“ 15,	—160 “ “ “ “	1/6 “ “	—Moderate chill
“ 16,	—165 “ “ “ “	1/4 “ “	—Severe chill

After these three injections the mode of administration was resumed as before.

Sept. 5, 1916—205 gr. Na I	intrav. c̄	1/3 gr. Hg Cl <sub>2</sub>	intramusc.—No chill
“ 6,	210 “ “ “ “	1/8 “ “	“ “
“ 7,	215 “ “ “ “	1/4 “ “	“ “
“ 8,	220 “ “ “ “	1/3 “ “	“ “
“ 9,	225 “ “ “ “	1/4 “ “	Chill
“ 10,	225 “ “ “ “	1/4 “ “	“
“ 11,	230 “ “ “ “	1/3 “ “	“
“ 12,	235 “ “ “ “	2/5 “ “	“
“ 13,	240 “ “ “ “	No Mercury	No chill
“ 14,	245 “ “ “ “	“ “	“ “
“ 15,	250 “ “ “ “	“ “	“ “
“ 16,	1.0 gm. salvarsan in foot caused phlebitis and necessitated rest.		

It will be seen from the above that chills develop much earlier when the mercury (1/5 grain) is given mixed with the iodide (160 gr.) intravenously than when given separately, the iodide (225 gr.) intravenously and the mercury (1/4 gr.) intramuscularly, and that on stopping the mercury no chills were produced even with larger doses of iodide (240, 245, 250 gr.), but later chills were produced by 310 gr. of iodide without any mercury.

## SUMMARY OF IODIDE TREATMENT

Started June 24, 1916, stopped February 3, 1917, (could no longer find veins).

Period of 224 days.

Number of injections, 125.

Amount of sodium iodide 26,013 gr. or about  $3\frac{3}{4}$  avoirdupois pounds or 1,685.7 grams.

Average dose for 125 doses, 208 gr. or 13.5 gm.

Average dose per day for entire period of 224 days, 116 gr. or 7.5 gm.

## PREPARATION OF SOLUTION

At first 5 per cent solution of chemically pure sodium iodide was made up in 0.9 per cent sodium chloride solution, but this latter was replaced later by distilled water, as it was found to possess no advantage over the plain solution and just added so much to an already hypertonic solution. It was also found by experiment that the iodide solution would stand boiling without any appreciable dissociation of sodium and iodide radicals, and consequently solutions could be sterilized in this way; further, that solutions of from 5 per cent to 10 per cent strength were correct—below 5 per cent too bulky; above 10 per cent too irritating. Large veins tolerate the concentrated solution, because here there is a large column of blood with which to mix, but when using very small veins the column of iodide solution practically replaces the blood, is undiluted and consequently irritating to the vein walls. The optimum strength for universal use is 8 per cent. A stock solution of sodium iodide in distilled water should be made so that one minim of the solution contains one grain of the salt and this carefully filtered. Of this solution the dose is measured and water (preferably freshly distilled) is added to make the desired strength and a moderate excess to allow for evaporation. The solution is then sterilized by boiling in a beaker or flask for ten minutes, and cooled to 105° F. when it is ready for injection.

*Technic:*—When the dose to be given is small and the amount of fluid not great, a large glass syringe of 20 c.c. to 50 c.c. capacity previously sterilized by boiling and a small hypodermic needle to fit should be used—preferably a needle of  $\frac{3}{4}$  in. to 1 in., and 22 to 26 gauge and with a short beveled tip. Where large doses are given an apparatus such as is adapted to salvarsan must be used and sterile

normal saline used in getting into the veins and in washing the apparatus afterwards, as leakage of iodide solution into the tissues is painful.

*Selection of Veins:*—The median basilic and median cephalic at the elbow are usually best adapted as they are superficial and relatively fixed in the tissues; but where a large number of treatments are required, veins must be sought for all over the body; at the elbow, forearm, wrist, hand, fingers, legs, also the external jugulars have rendered good service in my experience. Veins vary greatly in their reaction to injections. Some will thrombose with the first injection, others will stand a dozen or more. A vein may thrombose and later canalise or it may obliterate permanently. The stronger the solution used the greater is the chance of blocking, but I have never seen embolism or other harmful results follow.

#### MODE OF ACTION

The therapeutic value of the iodides in tertiary syphilis is so firmly established as to need no further proof or elaboration here; that lowly organized exudates, round cell infiltrates and gummatous masses often (not always) melt away as if by magic under full doses of the iodides is well known to anyone familiar with the subject. That these changes are the result of the action of the iodides on these poorly organized structures causing ultimate absorption in this way is probable. A direct action on the *treponema pallida* is not probable, for the experiments by Akatsu with iodide of sodium and potassium on these parasites, *in vivo*, show very weak spirocheticidal powers (1 to 10) for these chemicals; but it is interesting to note that the parasites do not acquire a great tolerance for these drugs (only 3 times) as against 35 to 70 times for mercuric chloride and 5 to 6 times for salvarsan when grown for some months in solutions containing these chemicals; but their beneficent effects are probably brought about by facilitating absorption of the masses in which the spirochetes are embedded and thus rendering the parasites more accessible to such drugs as salvarsan and mercury. Experiments by Kepinow suggest that the iodides act by favoring or accelerating autolysis of these tissues; Loeb found that iodides accumulated in greater concentration in syphilitic glands than elsewhere in the body, suggesting a selective affinity for syphilitic processes, and Pauli demonstrated that iodides lessen the viscosity of colloids, as these render protein solutions more fluid and

perhaps in this way favor solution and absorption of syphilitic deposits.

#### ABSORPTION AND EXCRETION

Iodides taken by mouth are well known to be, ordinarily, promptly absorbed from the stomach and small intestines, appearing in the secretions in from five to ten minutes, notably in the saliva. Excretion takes place chiefly through the kidneys, the drug appearing in the urine within ten to twenty minutes, reaching a maximum in two hours; sixty-five to eighty per cent, is excreted in the first twenty-four hours, but iodide is present in the urine from two to seven days or more, depending on the size of dose given (Cushny and Sollmann).

Mendel found that intravenously introduced sodium iodide was excreted more gradually than when taken by mouth. In healthy persons who served as tests a dose administered by mouth left the body in many cases several hours sooner, in one instance fully ten hours sooner than the same dose injected into the blood stream of the same individual.

It is a frequent occurrence to have a patient remark within a few minutes after beginning the injection that he can taste the drug in his mouth. The superiority of intravenous over oral administration of the iodides in this obstinate case is probably explainable on the basis of a prolonged mass action resulting from a large amount of iodide entering the blood and circulating in a concentrated form for a prolonged period. Certainly much larger doses can be tolerated by the intravenous route and iodism is much less apt to appear than after oral administration. Klemperer gave to paretics doses up to 50 gm. on alternate days with good results and without objectionable side actions. Prompt and favorable results were reported by Doeven-speck in 1905, in four cases, including a primary lesion in a man of 45 years; secondary cutaneous syphilide and mucous ulcer in a woman of 30 years; a patient with bony lesions and mucous ulcers; another with cerebrospinal syphilis; all of whom received doses of 0.1 gm. potassium iodide in 5 per cent solution daily for six days, these small doses proving sufficient for marked improvement. Mendel, in 1908, used sodium iodide in doses up to 0.6 gm. in 20 per cent solution for patients suffering from goitre and arteriosclerosis with satisfactory results. Lydston in 1914, speaks of excellent results obtained by the use of iodide in combination with mercury (mixed treatment). A

typical case of syphilitic pachymeningitis under his care, after failing to improve under the ordinary mercuric iodide and neosalvarsan treatment, was benefited by three injections combined with one grain of mercuric chloride. On three consecutive days this patient, who ultimately recovered, was given 120 gr. sodium iodide, and on the two succeeding days, 180 grains of potassium iodide, each dose was combined with one grain of mercuric chloride in ten fluid ounces of water. On the basis of favorable experience with intravenous iodide medication, Lydston recommends it in chronic rheumatism and related conditions. Intravenous iodide injections are considered by him as not only harmless, but actually superior to other channels of administration. Klemperer, a more recent contributor to the subject (1915), used sodium iodide intravenously in 10 per cent strength, finding that doses of 5, 10, 15 and 20 gm. were readily tolerated. Patients having general paralysis received large doses of 30, 40, 50 gm. usually repeated two or three times weekly without serious sequelæ of any kind.

Sometimes transitory reddening of the face and conjunctivitis were noted or slight headaches were complained of. It is specially noteworthy that he was enabled to continue intravenous injections of iodide after the oral administration of the drug had to be suspended on account of the onset of symptoms of iodism. On the basis of favorable experience with over 100 intravenous injections, this mode of administration is now extended by him to all cases of internal syphilis (of the central nervous system, tabes, circulatory organs, liver, etc.,) in five to ten gram doses. Pereira, in close touch with Klemperer's work, employed intravenous sodium iodide therapy, 10 per cent solution in doses of 10 to 30 gm. with excellent results, especially in cases of general paresis and tabes, with relief of lightning pains and parasthesias. A parietic patient, who was strikingly benefited by the treatment, received a total of 475 gm. of sodium iodide in 22 injections over a period of 47 days, without manifesting the slightest evidence of iodism. A return of memory and improved power of motion followed. Da Matta (1916) having used many dozens of injections in doses up to 20 gm. enthusiastically concludes that sodium iodide injections are most beneficial, the dosage not to exceed 15 gm. without special reason, and practically never causes troublesome manifestations of any kind. He emphasizes that patients do not lose weight when taking iodides in this way. Simon (1917), finding that his patients were not taking the iodides as prescribed, gave potassium



iodide intravenously, starting with 0.05 gm. and reaching 0.9 gm. in twenty-five per cent solution, with satisfactory results from every point of view.

*The indications for intravenous iodide treatment* may be summarized as follows:

Wherever the full iodide effect is required.

Where iodism develops before the desired result is obtained, iodide may be continued intravenously.

Unconscious patients or those unable to swallow.

Late internal syphilis, tabes, paresis, cirrhosis of the liver, aortitis, etc.

Where mouth medication fails to be effective and symptoms progress as in the case here reported.

It is doubtful if there are any *contraindications*, except lack of positive indications.

# CONCLUSIONS

1. Sodium iodide intravenously is harmless, and undoubtedly superior to both the potassium and the sodium salt given by the mouth. It contains relatively more iodine than the potassium salt.

2. Sodium iodide can be given in much larger doses than the corresponding potassium salt and is not depressing to the heart muscle, as is the case with potassium iodide.

3. It is better tolerated intravenously than by mouth and can be given in larger doses. The treatment is administered daily.

4. Patients often prefer the intravenous mode of administration.

5. A solution of from 5 to 10 per cent strength is correct and its injection painless.

6. No reaction appears until large doses are reached, and iodism is rare.

7. Intravenous dosage, 10 to 335 gr.

8. Chills started at 225 grains and have been reported by no other observer.

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## EPOCH-MAKING CONTRIBUTIONS TO THE STUDY OF SYPHILIS

### III. FRITZ SCHAUDINN AND ERICH HOFFMANN

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#### **Preliminary Report on the Occurrence of Spirochetes in Syphilitic Disease-Products and in Papillomata\***

(Received for publication, June 17, 1918)

AT the request of the President of the Imperial Health-Office, Dr. Koehler, and with the collaboration of Professor E. Lesser, investigations were begun in association with Drs. Neufeld and Gonder into the occurrence of microorganisms in the disease products of syphilis. As a result Schaudinn found in both natural and stained preparations, organisms which must be placed in the family of the spirochetes. The systematic affiliation of this family with the race of Protozoa has been maintained by Schaudinn by reason of his investigations into the *Spirocheta ziemanni* of the German stone owl.

Thus far the spirochetes can be demonstrated not only on the surface of the secreting efflorescences but also in the depths of the tissues and in the syphilitically affected inguinal glands.

In order to make possible the prompt verification of this find, it will be briefly imparted with the addition of two microphotographs. In addition to cases of pure syphilis others were studied which were complicated with other affections, and finally a research was made into the genitals of patients who were not suffering with syphilis, for the occurrence of similar organisms.

In the following lines the methods employed for investigation and the qualities of the parasites will first be depicted, followed by

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\*Arbeiten aus den Kaiserlichen Gesundheitsamte, 1905, xxii, p. 527.

an outline of the most important of the cases studied with addition of the parasitologic finds.<sup>1</sup>

For the discovery of the extremely delicate weakly refractive, but at the same time very actively moving spirochetes in the syphilitic tissues, the natural fresh material is most suitable. This should be examined at once upon its removal from the human body, in ordinary cover glass smears. In primary lesions, broad papules and condylomata immediately after excision a little tissue juice is obtained from as near the center as possible and placed on a cover glass which is then covered; lymph-nodes are excised outright and a drop of gland juice taken from the center of the rapidly incised gland.

For the demonstration of the spirochete in stained specimens one prepares the thinnest possible cover glass smears from the same regions of the morbid tissues and fixes them after they are air-dry in absolute alcohol for ten minutes. With reference to tingibility the spirochetes show different behavior in the individual case. In comparative studies one may isolate two series of forms, one of which is characterized by a higher refractive index during life of the spirochetes together with a firmer shape and for the most part broad shallow windings. In sections they stain well with the well-known spirochete stains (gentian-violet, carbol-fuchsin, Romanowsky stain, etc.) and are readily demonstrable. In the lists of cases these forms are designated as "dark colorable type;" they have not yet been found in pure syphilitic products but invariably in pointed condylomata (5 cases). The second group of forms comprises spirochetes which *in vivo* were extremely delicate and weakly refractive but for the most part provided with abrupt and narrow windings. To the ordinary stains they are not readily demonstrable and thus far we have been able to bring them out only through a strongly modified Giemsa azure-eosin stain in which well fixed cover glasses were left for 16-24 hours in the following mixture, always freshly prepared:

1. Twelve parts Giemsa's eosin solution (2.5 c.c. 1 per cent eosin solution to 500 c.c. water).
2. Three parts Azure I (aqueous solution 1:1000).
3. Three parts Azure II (aqueous solution 0.8:1000).

<sup>1</sup>The parasitologic statements in this work are from Schaudinn, and the clinical and literary ones by von Hoffmann. We are under obligations to Dr. Gonder for zealous collaboration in the preparation, staining and inspection of the specimens.

After brief rinsing with water the cover glasses are to be dried and enclosed in oil of cedar. Preparations of this kind show the second type of spirochete far more faintly than the first, but distinctly enough to be visible in a photograph (compare the two text figures). In the lists of clinical cases this form of spirochete is designated as "pale type," and is to be found in all purely syphilitic products.

Other certain distinguishing marks between these two groups have not thus far been brought to light. Only the study of the development of these parasites can teach us whether there are or are not two different species<sup>2</sup> involved. Following is a description of the pale variety.

The length varies from 4 to 10 microns, the average being about 7 microns as shown in a comparison of the spirochetes with the blood corpuscles in their midst. Our form should therefore be smaller than most varieties (spirochete obermeieri, ansernia, zie-manni, buccalis). The width varies from immeasurable to half a micron in the thickest of the dark type. The number of windings varies from three to twelve. The movements are those characteristic of the spirochetes as contrasted with those of the spirilla and are of three types: rotation about the longitudinal axis, to-and-fro movements and flexion movements of the entire body. The suggestion of an undulating membrane is at times present, but not of flagellation. The poles have pointed ends. In regard to the finer structure, especially of the nucleus, the investigation is very difficult and owing to the minuteness of the picture is not yet completed.

Dilution of the tissue juice with physiologic salt solution is well borne by the spirochetes which in one case were mobile after six hours. Upon addition of concentrated glycerin they varied in their behavior; some did not become immobile until after five to ten minutes, then becoming rigid in an immobile, corkscrew-like shape, to disappear finally after from one to two hours. Other individuals lost their wavy appearance immediately under observation and became quite straight; then gradually the rod shrank to a short spindle, recalling the malarial sporozoites. In one case

<sup>2</sup>Should the supposed differences in kind between the two forms be confirmed, I (Schaudinn) propose, for enrollment in the zoological system, the name of *Spirochete pallida* for the pale form, and for the dark-stainable form the name *Spirochete refringens*.

which was carefully observed, the shortening progressed to the formation of a short oval. Forms of this sort<sup>3</sup> were found after twenty-four hours treatment with glycerin. The cases investigated are as follows:

#### A. PURE CASES OF SYPHILIS

CASE 1.—A. K., twenty-five years, single, female, never ill before; since Jan. 20, 1905, hard, painless nodule on left labium majus; since about Feb. 22, eruption and headache.

Finds on Mar. 3, 1905; papulosquamous syphilide, general indolent adenopathy; on the left labium majus a well marked primary lesion, and several papules on the genitals which were but slightly eroded on the surface.

There was therefore an uncomplicated syphilis about two and a half months old. Before beginning mercurial treatment, on Mar. 3, a lentil-sized, hardly eroded papule was excised from the right labium majus. In the smears from the basal surface and center of the lesion were found quite numerous spirochetes of the pale type (about one individual to every fourth field).

CASE 2.—M. G., fifty-eight years, widow, never ill before; time of infection probably end of November, 1904; eruption since beginning of February, 1905.

Finds on Mar. 14, 1905: maculopapulous syphilide, numerous button-shaped, elevated, in part eroded papules on the genitals, multiple, indolent adenopathy.

Here we also have an uncomplicated case of lues about three and one-half months old.

On March 4, before treatment was begun, two lentil sized papules, not distinctly eroded, were excised from the labia majora. In the smears from the papules were found a few spirochetes of the pale type.

CASE 3.—L., age twenty-five, female, single, never before ill; infection probably end of November, 1904; middle of December, painless inguinal adenopathy; beginning of Feb., 1905, eruption and sore throat.

Finds March 15, 1905; general indolent adenopathy, maculopapular syphilis, papules on the genitals, tonsils and mucosa of the mouth.

Therefore in this case there was an untreated and uncomplicated syphilis about three and one-half months old.

For study there was removed on March 15, a noneroded, button-shaped, lentil-sized lesion from the labium majus. In smears from this papule numerous pale spirochetes could be demonstrated.

CASE 4.—A. K., age twenty-two, female, single, always healthy; probably infected middle of November; in December, hard nodule on the left labium; since middle of January, 1905, general phenomena.

<sup>3</sup>Whether or not we have to do here with a stage of latency of the spirochetes can only be decided by protracted, comparative studies of the development of the different spirochetes. The author knows of similar stages in the *recurrens* spirochete in the spleen of the patient and in the intestine of the bedbug host. His previous investigations, not yet published, into the spirochetes of birds and mankind have, however, showed him that similar stages can take very different routes of development.

Finds Mar. 20, 1905; universal seleradenitis; maculopapular exanthem, specific angina, alopecia, moist papules on the genitals.

Here therefore we also have an uncomplicated case of syphilis about four months old.

For study there was removed on March 21, before treatment was begun, a lentil-sized eroded papule from the labium majus. In smears from the papule extremely numerous pale spirochetes could be demonstrated. Photograph I came from this case.

CASE 5.—W. D., age twenty-seven, male, always healthy, infected end of July, 1901, toward end of August a pea-sized, somewhat moist nodule on the skin of the penis and soon afterwards painless inguinal adenopathy.

Finds on September 21, 1901: well developed typical primary lesion the size of a bean on the skin of the penis, hard dorsal lymphatic cord, indolent inguinal adenopathy, bilateral.

On September 24, the patient having received no treatment, the primary lesion and an inguinal gland of almost hazel nut size were extirpated.

Here was a fresh, uncomplicated syphilis, from seven to eight weeks old, in which general phenomena had not yet developed.

This case is of especial importance for our investigations. In 1901 Hoffmann had stained sections of this primary effect and gland, also numerous fine smears, with the most varied methods, without having been able to demonstrate micro-organisms of any kind. In order to have for future study, especially for confirmation, unobjectional material, he preserved along with the paraffin blocks a large number of cover glass smears which he stained after the discovery by Schaudinn of the spirochetes. To obtain the smears small bits of the interior of the gland and under surface of the primary lesion—which had been separated from the eroded upper surface by a smooth section—were wiped upon cover glasses. In this way the contamination with germs from the secreting surface was avoided. In the smears of both primary effect and gland numerous pale spirochetes were found. Photograph 2 was prepared from a gland smear from this case.

CASE 6.—v. K., age twenty-one, male; gonorrhea 1 year ago; otherwise always well. Infection Feb. 25, 1905; middle of March two sores on the foreskin, gradual painless adenopathy.

Condition April 3, 1905: lentil-sized primary lesion on the margin of the prepuce, another pea-sized one beside the frenulum, and a nonindurated erosion on the glands; typical indolent adenopathy in the groin.

Here we have undoubted, uncomplicated, syphilis only five and one-half weeks old.

On April 3, both primary lesions were excised and the attempt made to obtain by aspiration with a Pravaz syringe some juice from the swollen inguinal lymph nodes. In the smears of the primary lesions were found scanty spirochetes of the pale type. The gland juice was strongly diluted with blood and thus far no spirochetes have been demonstrated therein.

CASE 7.—P. L., male, twenty-three, always healthy. Infection with syphilis

probably in October, 1904. End of November an inunction cure (120 gms. grey ointment); since Mar. 20, 1905, sore throat.

Condition April, 1905: maculopapular, in part annular, syphilide, specific angina, plaques in mouth, eroded moist papule at anus.

The secretion from the anal papule of this subject, now ill for about 6 months with syphilis, contained in the fresh preparation scanty spirochetes of the pallid type.

#### B. CASES OF SYPHILIS COMPLICATED WITH OTHER AFFECTIONS

CASE 8.—E. F., twenty-four, male, always well. Infection about Feb. 15, 1905; four or five weeks later, hard ulcer in sulcus. Thus far no treatment. Condition April 4, 1905; in the coronary sulcus a pea-sized, shallow, readily bleeding ulcer with typical indurated base; prepuce retracted with difficulty, balanitis; bilateral bean-sized inguinal lymphnodes, indurated; moderate generalized adenopathy.

Here we see a case of syphilis 7 weeks old, complicated with balanitis. From the secretion of the primary lesion fresh sections and smears were prepared and the presence of both types of spirochete (pallid and dark-staining) in very large numbers was established.

CASE 9.—M. G., twenty, male, always healthy; admitted to Charité Hospital March 10, 1905, with two chancreoids and a right-sided bubo. The time of infection could not be determined. The chancreoids healed under iodoform and the bubo was treated by Lang's method. Upon the scar of the chancreoid there gradually developed a typical induration with central erosion on the inner aspect of the prepuce; the left inguinal glands were swollen, hard and indolent.

The lesion was a syphilitic primary lesion preceded by a chancreoid. It was excised on Mar. 25 for examination. At this period the chancreoid was already healed, so that the chancre could be regarded as purely syphilitic. The tissues contained pallid spirochetes in all smears.

CASE 10.—M. K., female, age twenty, always well. Infection probably in April, 1904. From June 20 to July 18 received fourteen injections of sublimate (to 0.02 gms.). Since middle of Feb. again ailing.

On Mar. 3, 1905, there were found present, in addition to gonorrhea, small papillomata and molluscum contagiosum with numerous shallow, button-shaped, raised moist papules on the genitals and the neighboring thigh with syphilitic angina.

The condition here is the first relapse of a syphilis which is almost a year old, complicated with an already long-existent gonorrhea, pointed condylomata and molluscum contagiosum.

Before beginning the second cure there was excised on Mar. 3, a good specimen of a lentil-sized papule having a somewhat gray deposit. The smears from the base of the papule showed a large quantity of microorganisms of various kinds, especially bacteria and only isolated spirochetes of the pallid and dark stainable types.

CASE 11.—E. W., female, age twenty, always well. Infected probably in October, 1904; end of December moist papules; no treatment so far.



Condition Mar. 30, 1905; notable inguinal adenopathy, specific angina, button-shaped moist papules on the genitals together with numerous papillomata.

This was four months' old syphilis, complicated later with condylomata acuminata.

On Mar. 30, smears were made from the secretion of the papule and a bean-sized hard inguinal gland extirpated. In the former were found numerous spirochetes of the dark stain type and sparse ones of the pale form. Smears from the inguinal gland contained only quite isolated individuals of the pale form and none of the other form.

CASE 12.—P. K., female, age twenty-three, never ill. Period of infection not accurately determinable. End of 1904 headache; beginning of January eruption. Feb. 28, admitted to Charité Hospital, where an exanthem and genital papules with scleradenitis were found.

No gonorrhea, no papillomata; after a sublimate injection cure, all syphilitic phenomena receded.

On April 3, 1905, smears were taken from the vaginal secretion. This case is then one of syphilis free from active manifestations and presenting a vaginal discharge. In smears from the latter no spirochetes could be found.

#### C. NONSYPHILITIC AFFECTIONS

CASE 13.—M., female, age thirty, denied syphilis; since December, 1904, vaginal discharge; since February, 1905, warts on the labia.

Condition Mar. 3, 1905: urethral gonorrhea, cervix catarrh, numerous quite large papillomata. Inguinal glands on both sides size pea to bean, not especially hard; no signs of lues, no suspicious history.

Here we have gonorrhea and condylomata acuta, which lesions could also have caused the adenopathy.

On Mar. 3, 1905, a wart was cut off for investigation. In the smears from the condyloma were demonstrated extremely numerous spirochetes of the dark, easily stainable variety.

Finally, we have undertaken a number of further investigations, concerning which we shall report briefly, without outlining the case histories. In one pure case of chancroid, no spirochetes were found in the secretions. In four pure cases of gonorrhea, the vaginal secretions were examined with negative result. Spirochetes were likewise absent in three cases in which, upon the discharge of cured cases of syphilis from the clinic, smears from the secretions of the genital mucosa had been made. In the smegma and vaginal secretions of six healthy subjects, no spirochetes were found. The control studies are to be continued. In a following report a more accurate account of these studies will be given.

The question now arises whether others have described similar parasites in the genitals. At the beginning of our investigations nothing was known by us of the occurrence of spirochetes in the genitals. Later Hoffmann found<sup>4</sup> that in 1891 "spirilla"<sup>5</sup> had been shown to be constantly present in balanoposthitis

<sup>4</sup>Berdal and Bataille: La balanoposthite érosive circinée. La Médecine Moderne, 1891, p. 340 etc. (review in Ann. de dermat. et de syph., 1891, p. 981).

<sup>5</sup>From the reviews which are at present accessible, it does not appear with certainty whether we have to do with spirilla or spirochetes. According to Czillag's leading statements the latter is the more probable.

circinata by Berdal and Bataille; and Czillag<sup>6</sup> had regularly found the same organisms in seven cases of this affection. The said, by no means common, affection is according to the experience of these authors contagious and can be artificially inoculated. Especially may it be emphasized that Berdal and Bataille made their inoculations only on syphilitic individuals, and that this affection may at times be accompanied with lymphangitis and indolent inguinal adenopathy. Both French authors further declare that in other genital affections, these spirilla are absent, or present only in slight numbers and in delicate form; while in balanoposthitis circinata they occur in abundance and even in sections are demonstrable between the epithelial cells. Czillag, who found that the length of the spirilla varied between 10 and 20 microns, and the breadth between 1-4 and 1-2 micron, and was able to stain them well with 5 per cent carbol-fuchsin, demonstrated them not only in the men with balanoposthitis but also in several women with discharge and erosions on the clitoris, but was unable to find them in the normal smegma.

More thorough investigations into the occurrence of spirilla in genital lesions were instituted by Rona.<sup>7</sup> In addition to hospital gangrene and other necrotising processes, he found them at times in normal smegma, often in the secretion of primary lesions (in ten of twenty cases), more rarely in moist papules (only two in eleven cases), and almost always in simple and circinate balanitis, never in uncomplicated chaneroid. He never made tissue smears of syphilitic tissues. It is worthy of mention that in syphilitic products of the buccal mucosa spirilla were almost always absent. The parasites illustrated by him, the systematic position of which is not discussed, appear to be considerably larger than those observed by us.

Whether the "spirilla" described by these authors have anything in common with those described by us in connection with syphilis must be learned from further study. For the time being we can establish the fact that in clinically unmistakable syphilis not only in the surface of syphilitic papules and primary lesions but also in the deep tissues and in indolently swollen inguinal lymphnodes true spirochetes may be demonstrated, in fresh and stained specimens, the technic of which has been related. Whether or not there are any distinguishing marks between the parasites of pointed condylomata and those of syphilis which can be brought to light, can only be shown by further research.

<sup>6</sup>Czillag: Spirillen bei Balanoposthitis, Arch. f. Dermat. u. Syph., 1898, xlvii, 150.

<sup>7</sup>Rona, S.: Der gangraenose, phagedaenische, diphtheritische Schanker der Autoren. Arch. f. Dermat. u. Syph., Bd. 1903, lxxvii, 259 and continued under another title in vol. lxxxi, 1904, p. 191 and vol. lxxiv, 1905, Nos. 2 and 3. Rona employs the designation "spirilla" and "spirochete" alternately; he mentions further, that Menge and Kroenig (1897) have found spirilla in normal vaginal secretions.

## PROFESSOR CHARLES PHILIPPE ERNEST GAUCHER

BY DR. GEORGES BAUDOUIN, PARIS, FRANCE

TRANSLATED BY JOHN E. LANE, M.D., NEW HAVEN

**C**HARLES PHILIPPE ERNEST GAUCHER was born July 26, 1854, at Champlemy, in the department of Nièvre. He was the second child of a family of five boys. His father, of Nivernais origin, was an architect in Paris; his mother was of Parisian birth.

Young Gaucher left Nièvre shortly after his birth but several years later returned and for a long time lived at Varzy with an uncle who was a physician and who fitted him for entrance into the Lycée Bonaparte at Paris, subsequently named Lycée Condorcet. Perhaps this long association with a country doctor gave birth to the inclination which later resulted in his choice of a profession. At any rate, after completing his classical studies at the Lycée Bonaparte, he began his medical studies. These were soon interrupted, for a year, by the requirements of the military service law. This enforced interruption did not completely sever his relations with medicine, for during this time he was successively attached as an attendant (infirmier) to two of the military hospitals of the Capital.

As soon as he was released from military service he enthusiastically returned to his medical studies and, eager for work, entered Milne-Edwards' Laboratory at the Muséum to prepare for his Licentiate in Natural Sciences. From this time he showed an especial aptitude for teaching. His ambition then was to obtain a position as teacher in a provincial School of Science. But he failed in his examinations for the Licentiate in Science, and this check, which compelled him to give up the project, exercised a decisive influence on his future.

From this time on, Gaucher devoted himself entirely to medicine, advancing with distinction from one rank to another. Intern of the Hospitals in 1877; as Chief of Medical Clinic from 1882 to 1884, he was the pupil of Potain, of Bouchard, of Landouzy, of Hillairet, of Fournier and of Bucquoy. He was Physician of the Hospitals

in 1886 and in 1892 became Physician of the Hospital Saint-Antoine and Professor *agrégé* of the Faculty of Medicine.

An excellent clinician, trained under the best teachers, he was the author of studies of justly deserved repute, especially those on "The Pathogenesis of the Nephritides," on "The Pathogenesis of Bright's Disease," and on "The Therapeutics of the Diseases of the Kidney." He devised a "Treatment for Diphtheria," which saved many lives previous to the discovery of diphtheria antitoxin by Roux. A little later he began to devote all his efforts to the teaching of dermatology and of syphilology. In 1885, he resumed studies which he had previously begun in collaboration with Hillairet, and with him published a "Theoretical and Practical Treatise of Diseases of the Skin."

When, as Professor *agrégé*, he had charge of the Supplementary Course of Dermatology and of Syphilography, he collected into one volume, entitled "A Treatise of the Diseases of the Skin," the lectures which he had given in this course at the Saint Louis Hospital. He also published several original articles, among them one on "Buccal Leukoplakia," and one on the "Histological Lesions of Pellagra," which were written in collaboration with Sergent.

In 1902 he succeeded Professor Fournier in the chair of Cutaneous and Syphilitic Diseases; in 1910 he became a member of the Academy of Medicine. During his fifteen years at the Saint Louis Hospital as Clinical Professor, he published numerous original articles, most of them on syphilis, especially hereditary syphilis; and a book, "The Elements (*Précis*) of Syphilography."

Although he had become a specialist by the fact that he had been entrusted with the official instruction in dermatology and syphilography, Professor Gaucher nevertheless insisted on remaining a physician in the general meaning of that word. Adhering to the theory of diathesis, which is in accord with the theory of the diathesis of autoinfection, advanced by Professor Gilbert, he always taught the importance which the consideration of the general health and of the terrain should hold in the study of cutaneous diseases. He used to say, "A specialist should be a specialist only when he has developed the specialty upon a broad knowledge of medicine" (*Le spécialiste ne doit être spécialiste que par surcroît*). This teaching is peculiarly French, and is well justified by the eminence of

the Dermatological School of the Saint Louis Hospital, whose representatives all are, first and foremost, *hospital physicians*.

Though an accomplished clinician, a perfect physician, in the full meaning of the term, Professor Gaucher often exhibited a scientific radicalism (intransigence) and a love of paradox, which was incomprehensible in a man of so great intelligence, and which led him to hasty generalizations which, however, did not diminish the value of his work.

Under a somewhat rough exterior, which made those who knew him but slightly judge him unjustly, there were hidden an excellent heart, an upright character, and absolute professional rectitude. Especially kind and considerate to the unfortunate, he unstintingly gave his charitable soul and zealously devoted himself to the organization and development of the Medical War Fund (Caisse Médicale de Guerre) which was established for the assistance of unfortunate confrères and of the widows and children of physicians who had been cruelly stricken by the war.

The energy which he displayed in this work in addition to the fatigue and strain which he had voluntarily taken upon himself from the very beginning of hostilities, by assuming the management of the Villemin Hospital, exhausted his strength.

The burden of so many obligations was too heavy for his sixty-four years. An attack of an acute pulmonary affection suddenly overwhelmed Professor Gaucher and after a few days, on January 25, 1918, he passed away, surrounded by affectionate friends.

## PROCAINE AND NOVOCAINE IDENTICAL

TO THE EDITOR:

It appears that in certain quarters the attitude is taken that the local anesthetic sold as Procaine is not identical with that marketed as Novocaine. The Subcommittee on Synthetic Drugs of the National Research Council believes it important that this misunderstanding should be corrected and hence offers the following explanation:

The monohydrochloride of para-amino-benzoyldiethylamino-ethanol, which was formerly made in Germany by the Farbwerke, vorm. Meister, Lucius and Bruening, Hoechst A.M., and sold under the trademarked name Novocaine, is now manufactured in the United States. Under the provisions of the Trading with the Enemy Act, the Federal Trade Commission has taken over the patent that gave monopoly for the manufacture and sale of the local anesthetic to the German corporation and has issued licenses to American concerns for the manufacture of the product. This license makes it a condition that the product first introduced under the proprietary name "Novocaine" shall be called Procaine, and that it shall in every way be the same as the article formerly obtained from Germany. To insure this identity with the German Novocaine, the Federal Trade Commission has submitted the product of each firm licensed to the American Medical Association Chemical Laboratory to establish its chemical identity and purity, and to the Cornell pharmacologist, Dr. R. A. Hatcher, to determine that it was not unduly toxic.

So far, the following firms have been licensed to manufacture and sell Procaine:

The Abbott Laboratories, Ravenswood, Chicago.

Farbwerke-Hoechst Company, New York, N. Y.

Rector Chemical Co., Inc., New York, N. Y.

Calco Chemical Company, Bound Brook, N. J.

Of these, the first three firms are offering their products for sale at this time, and have secured their admission to New and Non-

official Remedies as brands of Procaine which comply with the New and Nonofficial Remedies standards.

While all firms are required to sell their product under the official name "Procaine," the Farbwerke-Hoechst Company is permitted to use the trade designation "Novocaine" in addition, since it holds the right to this designation by virtue of trademark registration.

In conclusion: Procaine is identical with the substance first introduced as Novocaine. In the interest of rational nomenclature, the first term should be used in prescriptions and scientific contributions. If it is deemed necessary to designate the product of a particular firm, this may be done by writing Procaine-Abbott, Procaine-Rector, or Procaine-Farbwerke (or Procaine [Novocaine brand]).

Julius Stieglitz, Chairman,

Subcommittee on Synthetic Drugs, National Research Council.

#### EDITOR'S NOTE:

The Federal Trade Commission recommends the use of the official name of the licensed drugs in connection with all written articles and advertisements, and if the proprietary brand name is to be used, to place this side by side with the official name.

The official names so far adopted by the Federal Trade Commission are:

*Arsphenamine* for the drug marketed as Salvarsan, Diarsenol, and Arsenobenzol, etc.

*Neoarsphenamine* for the drug marketed as Neosalvarsan, Neodiarsenol and Novarsenobenzol, etc.

*Barbital* for the drug marketed as Veronal.

*Barbital-Sodium* for the drug marketed as Medinal and Veronal-Sodium.

*Procaine* for the drug marketed as Novocaine.

*Procaine Nitrate* for the drug marketed as Novocaine Nitrate.

*Phenyleinchoninic Acid* for the drug marketed as Atophan.

# Abstract of Current Syphilis Literature

It is the purpose of this JOURNAL to review so far as possible all literature on syphilis as it appears in other medical periodicals and to present it in abstract form. Authors are requested to send abstracts or reprints of their papers to the Associate Editor, Dr. Wm. H. Deaderick, Dugan-Stuart Bldg., Hot Springs, Arkansas.

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WM. H. DEADERICK, M.D., EDITOR

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POSTCONCEPTIONAL SYPHILIS.—Villapadierna, Madrid. *El Siglo Médico*, 1918, vol. lxxv, p. 122.

The author reports seven cases of this incidence, three of which occurred in a maternity hospital before the day of the Wassermann. Each woman was surely infected during pregnancy, for the traces of the chancres were apparent. The child of the first mother was free from any evidence of the disease and the placenta was normal. The mother had been infected in the fifth month and had received an inunction cure. The second woman was infected about the third month and also received a friction cure, but the fetus was born dead and macerated. The third mother was infected in the fifth month, no treatment being mentioned. The child was born alive with active manifestations of syphilis. The other series of four women was studied with Wassermann control. The patients were all infected during pregnancy. In the first two there were evidences of recent syphilis, both infants being syphilitic, one stillborn. The third patient presented only gonorrhea clinically and the Wassermann was at first negative. Later papules appeared about the anus and the reaction became positive. The infant gave a positive on the second trial. The fourth woman presented evidences of severe syphilis and received an injection cure of mercury cyanate. Her infant was born sound, but died soon of enterocolitis. Autopsy revealed the presence of visceral syphilis.

THE PRESENCE OF SPIROCHETES IN THE KIDNEY.—Yutaka Kon and Tomomitsu Watabiki, Tokyo, Japan. *Journal of the American Medical Association*, 1918, vol. lxx, p. 1523.

By Levaditi's method the authors have found many spirochetes in the hyaline casts and hyaline substances in urinary tubules, without



relation to any diseases. Further and more minute attention must therefore be paid to the study of spirochetes in the kidneys. The spirochetes are found not only in the casts, but also in the hyaline or granular substances located in the cortical substances, in urinary tubules, in Bowman's capsule, and in cysts. But they have not yet been found in the blood vessels, in the interstitial tissues, or in the cells. The spirochetes may be divided into three types: Type I is much like the *Spirochete pallida*, particularly in its spiral form. Type II shows an irregularly curved spiral, while Type III is much broader than Type I or II, and its curves are much coarser and less regular.

GENERAL CHARACTERS AND EVOLUTION OF SYPHILITIC CHANCRE IN THE ARAB.—Lacapere. *Annales des maladies veneriennes*, 1918, vol. xiii, p. 80.

While syphilis is very common in the Arab, the initial lesion is seldom seen, and hence timely treatment is usually out of the question. The Arab is, of course, circumcised, so that the scar left by the chancre will be on the glans or in the furrow. He is dirty in his habits and this fact together with the exposure of the glans to friction, causes the virus to be implanted in several excoriations at once. There may be a large, irregular sore, with a polycyclic border, or several distinct lesions. The ulcerated surfaces are apt to be covered with crusts, grayish or yellow. Doubtless from mixture of infection the buboes frequently suppurate. The scar of the chancre is free from pigment and surrounded by a brown ring. The author in his years of experience has seen but 125 chancres in Arabs, of which 16 were hybrids with chaneroid and 15 extragenital. Of the 125 cases 55 were seen in women, the ratio of chancre in this sex being therefore high.

SYPHILIS OF THE HEART AND AORTA.—Bryce W. Fontaine, Memphis, Tenn. *Southern Medical Journal*, 1918, vol. xi, p. 278.

The records of the Memphis General Hospital for the years 1916 and 1917, inclusive, show a total admission of 219 cases of cardiovascular disease, among which were 43 whites, 176 negroes, 183 males and 36 females, between the ages of 4 and 77 years. Among these patients, disease of the cardiac valves heads the list with the occurrence of mitral insufficiency in 133 of the cases, and aortic insufficiency in 24. Next in point of number were aneurysms of the aorta and the peripheral arteries, of which there were 18. The etiologic factors in these cases were determined by means of a careful history, physical examination by several attendants, examination with the Roentgen ray by plates and fluoroscopy, bacteriologic, and serologic examinations of the blood and spinal fluid, and by postmortem examination. Such a study showed in the case of mitral diseases, 37, or 27.8 per cent, infected with

syphilis in the case of aortic diseases 11, or 45.8 per cent; and in the case of aneurysm 11, or 61.1 per cent. From this can be seen how very prominent and common a factor syphilis is in the production of diseases of this character. Careful study of the cases will show a uniform tendency of all varieties to affect the young adult. Signs of the disease usually appear before the thirty-fifth year, within an interval of from ten to fifteen years after infection. However, there are exceptions as the author has personally observed two patients in whom it developed within two or three years after infection. In recognizing cases of cardiac syphilis, too much stress can not be laid upon the value of a routine Wassermann test of the blood in all cases of cardiovascular disease; when the test is negative, a cell count and a Wassermann upon the spinal fluid should be made. In all cases presented for physical examination we should not fail to examine the pupils for the Argyll-Robertson reaction and the knee jerks. The presence of the first is confirmatory, and the absence of the second is suggestive of syphilis of the nervous system which could very easily be associated with the same disease in the cardiovascular system.

THE ROLE OF SYPHILIS IN SURGERY.—George Gellhorn, St. Louis, Mo.  
Southern Medical Journal, 1918, vol. xi, p. 369.

Two ways by which surgical patients may come to harm on account of their syphilis immediately suggest themselves. The first is the possibility that such patients, through errors in diagnosis, are subjected to unnecessary, and even dangerous operations. That mistakes of this kind occur is, after all, not surprising. A disease like syphilis, which appears in a thousandfold deceitful disguises, might well produce manifestations which resemble conditions calling for operative intervention; and, indeed, there is hardly a surgical affection of any part of the body that at one time or another has not been mimicked by syphilis. As a result, superfluous operations a plenty have been performed. The second part of the inquiry has to consider patients with unrecognized or untreated syphilis who are subjected to operation on very good surgical indications. The number of such patients is probably very large. Do they run any undue risk in surgery? Is their syphilis likely to lessen their chances of ultimate recovery or to interfere with the normal course of convalescence? Theoretically, an affirmative answer to these questions seems self-evident. We know that syphilitic infection causes a generalized spirillosis almost instantaneously. We know, furthermore, that in syphilis the blood channels and the heart suffer the greatest involvement and that the heart is probably the most frequently affected organ of the body. Of other vital organs the kidneys may become acutely or chronically inflamed in syphilis. In fact, all organs and tissues of the body may be more or less affected by lues, and the syphilitic cachexia which we find so frequently, and more particularly in women, is by no means confined

to the later stages of the disease, but is often encountered, for reasons as yet unknown, in young women who have latent syphilis. Syphilis as an etiologic factor in surgical mortality does not ordinarily receive the consideration it deserves.

**SYPHILIS OF THE LUNG.**—J. A. Witherspoon, Nashville, Tenn. *Southern Medical Journal*, 1918, vol. xi, p. 275.

While no tissue is immune to syphilis, the lungs are less frequently involved than other organs in the human body. Pathologically, the most simple division is in three forms: The gumma, which is usually multiple and may be bilateral; the pneumonic where there are marked changes in the connective tissue with intense cell proliferation filling the alveoli and infiltrating the septa, peribronchial and perivascular tissues. The third pathologic type is the fibrous with increased connective tissue with a misshaped sclerosed lung as the result. This type does not yield very readily to treatment. The treatment is the same as syphilis in any other viscus. The writer prefers mercurial ointment in the most vascular parts, such as the inner sides of the thighs, axillæ, etc., combined with ascending doses of iodides. Salvarsan is valuable temporarily, but can not be depended upon for a cure.

**GUMMOUS SYPHILIS OF THE THYROID GLAND.**—Francis Eugene Senear, Ann Arbor, Michigan. *The American Journal of Medical Sciences*, 1918, vol. clv, p. 703.

Gummatous syphilis of the thyroid gland is of rare occurrence. Women are more frequently subjects than men. The cases so closely resemble carcinoma clinically that a differential diagnosis on these grounds alone is often impossible. The usual change is a hard, nodular or smooth tumor involving either lobe, the isthmus or the whole gland. Symptoms due to thyroid disturbance are unusual, and when they occur are those of myxedema, or apparently rarely those of hyperthyroidism. Symptoms due to interference with respiration are very common, and may be so severe as to cause death. If the patient is seen before death is imminent and antisiphilitic treatment instituted, the prognosis is very good.

**SYPHILIS OF THE STOMACH AND INTESTINES.**—Sidney K. Simon, New Orleans, La. *Southern Medical Journal*, 1918, vol. xi, p. 280.

Prior to the last decade, involvement of the stomach and the upper intestinal tract in syphilis had been considered among the rarest of the clinical manifestations of the disease. The marked awakening of interest in the condition and its more universal recognition at the present time may be traced to the influence wielded in the main by

two factors: (1) The widespread employment of the Wassermann reaction in recent years and the greater facility with which syphilitic disease in general may now be diagnosed; (2) the present extensive use made of the roentgen rays as a further means of interpreting the more obscure and definite types of abdominal disease. The diagnosis after all must be made to rest on a correlation of the more important clinical and laboratory data. This includes the most essential factors, a history of previous infection in the patient; the evidence of syphilitic lesions perhaps in other parts of the body; the finding of a positive serum reaction in the blood or spinal fluid; the results of the roentgenologic examination; and, finally, the beneficial effects derived from antiluetic treatment.

**CARDIAC SYPHILIS.**—William Cabell Moore, Washington, D. C. *The American Journal of Medical Sciences*, 1918, vol. clv, p. 667.

Cardiac complications during syphilis occur much more frequently than has been recognized generally heretofore. The cardiac lesions occur earlier in the disease than has been thought, even in the early secondary stage. Congenital syphilis of the heart is a cause of sudden death in early life, this condition being unsuspected clinically, as a rule. The nature of the process in the heart is distinct and may be recognized microscopically, and the spirochetes may be found in the lesion; it is most frequently a myocarditis. Uncomplicated aortic insufficiency is of syphilitic origin in the majority of instances. Two symptoms are not definite, but extremely suggestive; the diagnosis depends mainly upon the signs of some cardiac disorder, with a positive Wassermann, and a response to antiluetic treatment. The prognosis is good in the early stages and varies directly with the stage of the disease and the extent of the changes produced. Treatment should be mainly antisyphilitic and intensive. Cardiac treatment is required rarely except in cases with decompensation. Once instituted treatment should be carried through persistently and uninterruptedly.

**THE NERVOUS MANIFESTATIONS OF SYPHILIS OF THE EYE.**—Joseph Collins, New York. *The American Journal of the Medical Sciences*, 1918, vol. clv, p. 649.

In 467 of 790 patients it was noted that the pupils displayed the Argyll Robertson phenomenon. It is interesting to note that in proportion to the thoroughness of examination of patients who have syphilitic disease of the nervous system is the increased frequency with which the Argyll Robertson phenomenon has been found. Indeed, it may be said that the only infallible sign of syphilis of the nervous system is the failure of the pupil which is not fixed mechanically to react to light. In the 790 cases upon which this study is based there was a history of diplopia in 150 cases, i.e., in about 20 per cent. In only one-

half of the number were there any evidences of third nerve involvement when the patient was examined. In our statistics the third nerve showed evidence of being partially or completely paralyzed in 62 instances, and it is interesting to note that it was only affected on both sides in 5 instances. Paralysis of the third nerve in syphilitic disease of the nervous system is not infrequently associated with disorder of the sixth nerve; very rarely with involvement of the fourth. In this series of 790 cases the sixth nerve was involved 31 times; it may have been involved in other instances and have been the cause of the diplopia; in these 31 instances it was affected at the time of examination. The fourth nerve is affected in cases of syphilis of the nervous system very rarely. In five instances only was any disorder of it recorded in these statistics. In one instance it was bilateral. In 95 cases of the entire number the optic nerve was found to be diseased, showing inflammation, choked disk or atrophy, neuritic or simple. Among the 20 cases of cerebral meningitis papilledema was encountered five times, and in 251 cases in which the diagnosis of cerebrospinal syphilis was made it was noted seven times; in every instance the choked disk was bilateral. It is interesting to note that in 9 of the cases diagnosticated as tabes or taboparesis there was either optic neuritis or choked disk. In only 1 case of general paresis was there atrophy of the optic nerve, and in this case the tendon jerks were exaggerated. One of the extraordinary and inexplicable things about general paresis is that it does not cause optic atrophy. The author has never seen an instance of disorder of the pupils caused by syphilis of the nervous system disappear spontaneously or under treatment. Some of the muscle paralyses yield to treatment readily, others are most rebellious. The important matter is to distinguish one from the other. In a general way it may be said that the vast majority of cases of muscle paralysis associated with symptoms that justify the diagnosis of meningitis, especially those coming on abruptly, yield to treatment or recover spontaneously. On the other hand, those due to nuclear lesion (which are apt to develop insidiously) are rebellious and unamenable, but the majority of permanent ocular palsies are not of nuclear origin. Multiple ocular palsies indicative of diffuse lesion are quite as likely to yield to treatment as single paralysis.

**SYPHILOPHOBIA.**—W. Knowsley Sibley, London, England. *The Urologic and Cutaneous Review*, 1918, vol. xxii, p. 329.

Cases of this disease may be divided into three groups: (1) Men who abstain from normal sexual relations, on account of the fear of contracting syphilis. (2) Men who themselves have a firm conviction that they have contracted syphilis, notwithstanding the fact that every intelligent and honest doctor whom they have consulted has failed to detect the slightest evidence of the disease, after most thorough and complete investigation and tests. (3) Men who have been told by

some ignorant or unscrupulous doctor that they have syphilis when they have not, and have become so obsessed by this view that no amount of scientific reasoning will ever convince them otherwise. The dread of contracting syphilis leads many men in the prime of life to a prolonged and unnatural abstinence, which sooner or later tells severely on the central nervous system, producing restlessness of spirit, irritability of temper, distraction of thought, insomnia, depression, high arterial tension, suicide. In other cases it induces to various unnatural outlets for their sexual passions. Some men who have a firm conviction that they have contracted syphilis, have never done so. Cases of this kind are extremely difficult to convince of the incorrectness of their own diagnosis, and they will be perpetually bringing forward, according to their own conviction, fresh proofs or evidence of the disease. The third class includes those unfortunate people who, never having had syphilis, have had this disease misdiagnosed by some incompetent or unscrupulous specialist, or general practitioner. In the author's experience the throat specialists are frequent offenders in this respect. The Wassermann reaction may be perpetually negative, but the patient has been told he has had syphilis, and there is no getting away from it; and for years afterwards, on the slightest suspicion of a sore throat, usually a simple tonsillitis, he at once returns to the throat specialist for further treatment, which, needless to say, is never refused.

SYPHILIS OF THE KIDNEY.—H. A. Fowler, Washington, D. C. *Medicine and Surgery*, 1918, vol. ii, p. 56.

During the period of incubation and especially associated with the appearance of the skin eruption, a slight but definite albuminuria occurs. Casts are never present, and other evidences of serious damage to the kidney structure are wanting. The albumin disappears rapidly under specific treatment. Acute and subacute syphilitic nephritis occur at any time after the initial lesion. A form developing within a few weeks after the chancre and before the outbreak of cutaneous manifestations has been described. Aside from the preroseolar nephritis, which is characterized by its early onset and the absence of grave constitutional symptoms, acute syphilitic nephritis occurs in association with, or subsequent to, the outbreak of the cutaneous lesions. This complication may develop any time during the first two years, and especially during the first year after the primary sore. The first symptom is usually edema of renal distribution. This develops rapidly and general anasarca may quickly result. Hematuria is the first symptom in some cases and may be severe. In other cases progressive weakness with anemia and loss of weight are the symptoms first noticed. The urinary findings resemble those found in the more common forms of acute nephritis. The diagnosis is based upon the following criteria: (1) The proof of recent syphilitic infection; (2) the association of

nephritic symptoms with the symptoms of recent syphilis; (3) the absence of other causes of nephritis; (4) the special features of the disease; (5) the urinary findings; and (6) the therapeutic test.

Mercury should be given by inunctions or intramuscular injection. The dosage should be carefully guarded at first to avoid kidney irritation and the production of mercurial nephritis. If salvarsan is to be of any benefit, the first injection will show it. It is suggested that injections should not be repeated under fifteen days. It is further evident that the more chronic cases are less favorably influenced by salvarsan. In certain cases of chronic parenchymatous and interstitial nephritis the etiologic factor must be sought in an antecedent syphilis. When the kidney lesion is associated with amyloid degeneration and symptoms of tertiary syphilis of other organs—liver, spleen, pancreas, aorta, etc.—the diagnosis may be fairly easily made. In the less chronic cases when the infection has occurred years before, the diagnosis is extremely difficult. All other causes of the disease must be carefully excluded. A very strong positive Wassermann reaction is suggestive. An abundant albuminuria persisting for a long period with lipoiduria, but without associated vascular changes, should arouse suspicions of syphilis. In long-standing cases with amyloid changes, little or nothing can be expected from specific treatment. Mercury should follow the administration of salvarsan. This is well borne if care is used in beginning with intramuscular injections of small doses of a soluble salt and follow this by inunctions.

Gummata of the kidney are habitually multiple, and vary in size from a hazelnut to a walnut. More rarely the whole organ is involved in a single large gummatous tumor. Syphilitic infection of the pelvis of the kidney is rarely observed. The association of syphilis, particularly congenital syphilis, with paroxysmal hemoglobinuria has long been noted. This relation is interesting since hemoglobinuria occurs in other protozoan diseases; for example, in piroplasma disease of horses and in malaria.

In early as well as late hereditary syphilis lesions of the kidney occur usually in association with specific lesions and congenital deformities of other organs and parts of the body. All varieties of nephritis are met with, but as a rule the kidney changes are overshadowed in importance by other manifestations of the disease. The treatment of the various lesions of the kidney occurring in heredosyphilis is in general the same as that for renal complications in acquired syphilis.

**CARDIAC SYPHILIS.**—William Cabell Moore, Washington, D. C. The American Journal of the Medical Sciences, 1918, vol. clv, p. 667.

Cardiac complications during syphilis occur much more frequently than has been recognized generally heretofore. The cardiac lesions occur earlier in the disease than has been thought, even in the early secondary stage. Congenital syphilis of the heart is a cause of sudden

death in early life, this condition being unsuspected clinically, as a rule. The nature of the process in the heart is distinct and may be recognized microscopically, and the spirochetes may be found in the lesion; it is most frequently a myocarditis. Uncomplicated aortic insufficiency is of syphilitic origin in the majority of instances. The symptoms are not definite, but extremely suggestive; the diagnosis depends mainly upon the signs of some cardiac disorder, with a positive Wassermann, and a response to antiluetic treatment. The prognosis is good in the early stages and varies directly with the stage of the disease and the extent of the changes produced. Treatment should be mainly antisymphilitic and intensive. Cardiac treatment is required rarely except in cases with decompensation. Once instituted, treatment should be carried through persistently and uninterruptedly.

**TUBERCULOSIS AND SYPHILIS.**—Edward von Adelung, Oakland, Cal. *Journal of the American Medical Association*, 1918, vol. lxx, p. 1211.

In 1914, of 34 cases of tuberculosis confirmed by the finding of tubercle bacilli in the sputum, 8 yielded positive Wassermann tests. This means that 23.5 per cent of syphilis was found during 1914 in laboratory-positive tuberculosis. Of these 8 cases of double infection, 78 per cent of the patients were female and 22 per cent male. In 1915, of 52 cases of positive-sputum tuberculous cases, 4, or 7.6 per cent yielded positive Wassermann tests. Of these 4 patients, 25 per cent were female and 75 per cent male. In 1916, of 61 cases of pulmonary tuberculosis, 2, or 3.2 per cent yielded positive Wassermann tests. Both of the patients were women. In 1917, of 48 positive-sputum cases of tuberculosis, 3 or 6.2 per cent, yielded positive Wassermann tests. Summing them up in four years, it is seen that of 195 cases of pulmonary tuberculosis confirmed by finding the bacilli, 17, or 8.7 per cent, yielded a positive Wassermann test. This represents what would be overlooked by the average practitioner when treating open cases of tuberculosis of the lungs without making the Wassermann test.

**GONORRHEA COMPLICATED BY SYPHILIS.**—N. P. L. Lumb. *The British Medical Journal*, March 9, 1918, p. 285.

In the past it has been customary to look upon syphilis as a much more important disease than gonorrhea, and considerably more attention has been paid to it than to the latter. This is evident from the fact that a patient presenting himself with signs of both syphilis and gonorrhea is commonly given thorough antisymphilitic treatment without delay, while the sum total of the treatment advised for gonorrhea is an irrigation twice a day with permanganate of potassium. This plan is unsatisfactory, and an experience of large numbers points to the fact that modern antisymphilitic treatment at times (1) stirs a la-



tent gonorrhea into activity; (2) leads to the development of complications; (3) renders the gonorrheal lesions very intractable. The proportion of cases in which untoward effects are noticed seems to be about 10 per cent, and, in consequence, the author has adopted the following routine in every case of syphilis, varying according to whether there are active signs of gonorrhea or a past history of it.

1. When there is a past history of gonorrhea and no active signs. (a) A six to eight hours' specimen of urine is taken twenty-four hours after the first injection of mercury and examined microscopically for gonococci after centrifuging. The presence or absence of threads is also recorded. (b) The prostate and vesicles are examined during the first week of treatment. A smear of the expressed secretion is made and examined microscopically for gonococci. If both *a* and *b* are negative a dose of gonococcal vaccine is given (50 million gonococci) and test (a) repeated twenty-four hours later. If no gonococci are found, no treatment is necessary. If gonococci are found, the urethra is examined carefully with the urethroscope to locate the infection, and suitable treatment commenced at once, varying with the nature of the lesion.

2. When there are active signs of gonorrhea. Irrigation into the bladder with 1:8000 potassium permanganate is commenced at once, the strength being rapidly increased to 1:4000 as soon as the patient can irrigate successfully. Vaccines are given from the start at regular intervals and the prostate examined about the tenth day. A straight bougie is passed at the end of the second week, and this reveals the presence of any inflamed glands of Littre.

**SYPHILITIC MULTIPLE SCLEROSIS—DIAGNOSED CLINICALLY IN SPITE OF NEGATIVE LABORATORY TESTS.**—Tom A. Williams, Washington, D. C. *Nashville Journal of Medicine and Surgery*, 1918, vol. cxii, p. 35.

The low lymphocyte count in the presence of such severe symptoms and the relative poverty of radicular signs indicate that the pathologic process causing the symptoms is within the central nervous system in the main, and not merely an involvement of the roots by an extension from the meninges into their coverings of syphilitic leptomeningitis, as in the case in *tabes dorsalis*. There are, in all probability, foci of ill-nourished, if not necrotic tissue, scattered throughout the central nervous system, perhaps as a result of endarterial proliferation which may have led in some cases to obliteration. In proportion as this is incomplete, and the tissue elements have not perished, there will be restoration of function, as tissue activity is resumed upon the removal of exudate from arterial wall or connective tissue, by the destruction of its cause, the *treponema pallidum*, by salvarsan or mercury.

In the presence of lesions of this character, the signs may lack all systemization, as in this case. In insular sclerosis it is rare that the mid-brain, or the pyramidal tract, escapes when the process is at all extensive. The absence of nystagmus and of extensor response of the toes immediately make the author suspicious of this diagnosis. The experimental therapeutics confirm the author's doubts; but unless the luetin reaction is regarded as pathognomonic, only an examination postmortem can give absolute proof; and in some cases even this has failed to distinguish between disseminated sclerosis of the usual type, and that sometimes believed to occur as a result of syphilis. It must not be forgotten that postmortem appearances are after all merely the results of the reaction of the body to insult, and that these results both resemble one another and vary so much that few of them are pathognomonic for any particular invasion. For instance, even plasma cells, so characteristic in paresis, merely denote chronicity, and may occur under many conditions quite irrespective of syphilis. Again, during life the reactions of the body to the particular noxa are by no means certain; otherwise we should not find Wassermann reaction absent in nearly 40 per cent of tabetics, and we should not find it present as a reaction to the organisms of leprosy.

SYPHILIS IN ITS RELATION TO INSANITY.—R. M. Phelps, St. Peter, Minnesota. *The Journal-Lancet*, 1918, vol. xxxviii, p. 221.

The Wassermann reaction is not yet a sure evidence of syphilis when present, and still less against syphilis when absent. It is true a large percentage of positive Wassermans are certain evidence; yet there is need of other evidence for particular cases. Confirmatory tests of finer definition are claimed, but statistics based on them are not extensive in statistical groups. Admitting the test to be certain, there is no surety that the following insanity is caused by it or in any way dependent upon it. Insanity is so prevalent that any causal connection is based on a very slight degree of probability. It is coming to be realized that a positive Wassermann is common in persons not insane; but opportunity to obtain general percentages of large groups has not yet been found. The conclusion is based largely upon those coming to hospitals for other troubles, and to a few collections in some homes for delinquents.

SYPHILIS IN RELATION TO MENTAL DISEASE.—William C. Sandy, Middletown, Connecticut. *New York Medical Journal*, 1918, vol. cvii, p. 734.

By far the most common type of psychosis due to syphilis is general paralysis of the insane, or paresis as it is frequently called. Often insidious in onset and protean in clinical manifestations, paresis may be unsuspected until the attention is forcibly directed to the unfortu-

nate individual by some scandalous action, or marked change in habits, disposition, or conduct entirely foreign to his ordinary mode of living. The disease is apt to make its appearance about the age of thirty-five to forty years, usually some ten years or more after the initial infection, the ordinary course being a progressive deterioration with death in from two to five years. Theoretically cerebral syphilis is to be sharply distinguished from paresis, but clinically the differentiation may be an extremely difficult matter. Cerebral syphilis may be said to be more on the surface as contrasted with the parenchymatous changes of paresis. There are three types, which may be combined to a certain degree; the gummatous, which is rarest, the meningeal and the vascular, the last consisting of a progressive, girdling, obliterating endarteritis. From the very nature of cerebral syphilis, it will be seen that symptoms of a focal variety, such as paralyses, are more apt to occur. *Tabes dorsalis*, or locomotor ataxia, the chronic progressive, deteriorating process of the posterior spinal nerve roots with syphilitic origin may be associated with a paranoid psychotic condition necessitating commitment to a hospital for the insane. Juvenile paresis is a most striking result of inherited lues. A child may develop apparently normally for a few years when not only further progress ceases, but there is a decided lowering of mentality. Epileptiform convulsions may lead to an erroneous diagnosis of epilepsy. Various puzzling symptoms such as states of fear, excitement or depression may arise, accompanied by gradual deterioration, resulting in death in three or four years. A careful neurologic examination with investigation of the blood and spinal fluid should clear up all mystery as to the diagnosis, and autopsy findings will show the changes found in the adult form of paresis. Psychoses of the manic depressive type comprise a small group in which the laboratory demonstrates a syphilitic etiology.

**TABES DORSALIS, STATISTICAL STUDY OF 240 CASES.**—Morris Grossman, New York. *The Journal of Nervous and Mental Diseases*, 1918, vol. xl, p. 92.

The average age of syphilitic infection, dated from the primary chancre, was 24.4 years. The average age of onset of *tabes* in 238 cases was 39 years. No detectable difference exists in the age of onset of *tabes* and those of patients treated with antisiphilitic remedies and in the age of onset in those untreated or presumably less treated. The average pre-tabetic interval is not greater than 14.6 years. The pre-tabetic in the young may, but seldom does, last for a shorter period than in the more mature. The resistance of the central nervous system seems to deteriorate with age. The duration of the pre-tabetic period may be influenced by age. The probable average pre-ataxic period is three years. Women seem to have a shorter pre-ataxic period than men. The average life expectancy of the bedridden tabetic is very

much longer than that usually taught. The average age of the immobilized tabetic is 53 years. Most tabetics usually perpetuate the ataxic stage; in the small percentage of cases which become bedridden, owing to uncomplicated ataxia, the average duration of the ataxic period is 4.11 years. Among those tabetics who become bedridden, a short ataxic period usually follows a short preataxic period. This substantiates Maloney's contention that the deterioration of attitude is mainly a mental and not a structural deterioration. The short ataxic period in these bedridden cases is due to the same mental inferiority as is conducive to the short preataxic stage. The cause of death in tabes is syphilis. Syphilis and tabes lead to death through cardiovascular and renal degeneration, and through weakened resistance to nonsyphilitic infections. The average age at which death occurs is 53 years. The mortality among tabetics over 53 years of age is 238 per 1,000. Tabes is as nonlethal as any form of syphilis.

JUVENILE PARESIS: A REPORT OF THREE CASES.—Rachel L. Ash, San Francisco. *Archives of Pediatrics*, 1918, vol. xxxv, p. 160.

In these three patients the disease appeared in early adolescent life at the ages of six, ten and fourteen, respectively. Congenital syphilis is probably present in all three. In all three patients loss of mentality accompanied by speech disturbances was noticeable at an early stage of the disease. Fixed and unequal pupils and hyperactive tendon reflexes were common to all. One patient has epileptiform convulsions, headaches and other equivalents; another has paralytic seizures. The complement-fixation test in the spinal fluid and blood was positive in the three cases. Nonne, Noguchi and pleocytosis were found in two instances and Lange's paretic curve once. If cerebral spinal syphilitic disease and brain tumor can be excluded from these three patients, the history of hereditary lues, the progressive loss of mentality, the altered speech, the unresponsive and unequal pupils, the hyperactive tendon reflexes, the positive Wassermann in the blood and spinal fluid, permit of no other diagnosis than juvenile paresis. Cerebrospinal syphilis, when a meningoencephalitis, appears clinically as congenital idiocy or imbecility; when a diffuse gummatous process, it betrays itself by constant pressure signs (choked disk, headache, convulsions, etc.) and otherwise by exacerbations, remissions and symptoms irregularly distributed in time and in locality. In brain tumor the early pressure symptoms are followed by localizing signs; the intelligence and memory are lost much later. Cerebrospinal syphilis and brain tumor may, therefore, be excluded from the three cases reported.

ON NEUROFIXATIONS.—Mallein, Tzanck and Kermorgant. *Annales de la dermatologie et de syphilographie*, 1917, vol. vi, p. 570.

The authors, all French military surgeons, describe a neurofixation as follows: a syphilitic consults during the first days of his disease and

receives a series of injections of one of the arsenical preparations, after which the chancre and exanthem disappear. Six or eight months later he returns with symptoms implicating the cranial or peripheral nerves, brain or cord, which prove to be singularly refractory to anti-syphilitic treatment. A neurofixation must not be confounded with a neurorecidive, for the latter is a somewhat vague, general term which could mean precocious nerve syphilis or arsenical poisoning. In a neurofixation the treatment has been insufficient or badly judged. The cause is not the spirochete alone, and not the arsenic alone, but the condition is a hybrid. The severity of the disease is not a factor nor is the particular preparation of arsenic, nor the presence or absence of mercurial treatment. In all cases seen the injections were given when the exanthem was in full bloom or before its appearance. The initial symptom is usually a severe, persistent headache of a special type, associated perhaps with neuralgia, paresis of the eye muscles, labyrinthine symptoms, etc. At times there are symptoms of pretabes. The blood Wassermann is not always positive, but in the cerebrospinal fluid the sum of the evidence always denotes syphilis. The totality of symptoms suggests latent or chronic meningitis. In a fatal case the meninges were found extensively involved. The treatment had been notably insufficient. In such cases we must differentiate neurofixation from pure syphilis on the one hand, and arsenical lesions on the other. This should not be difficult, but the pathogeny of the neurofixation remains obscure. There is a certain parallelism, however, between it and Herxheimer's reaction. Both appear after insufficient treatment with arsenic. Neither appears if treatment is begun before the twentieth day of the chancre. Both are rebellious to treatment.

**SACRAL TABES WITH THE CLINICAL PICTURE OF A LESION OF THE CONUS MEDULLARIS.**—G. B. Hassin, Chicago. *Journal of the American Medical Association*, 1918, vol. lxx, p. 755.

Cases of sacral tabes have an enormous scientific and practical value. Their scientific value lies in the fact that they afford unusual opportunities for studying the probable course of the sacral root fibers within the spinal cord, the nature of some ascending and descending fasciculi, etc., a matter of great interest. The practical value is due to the fact that some cases of so-called conus lesion may be nothing but tabes. So far this case is the only one on record that strongly suggests such a possibility. The very few cases of sacral tabes, reported up to the present time, differed from this by the presence of some classical signs of tabes (Argyll Robertson pupil, loss of knee jerks, etc.) which, as the author pointed out, were totally absent in their patient. The trophic disorders on the buttocks and heels they ascribed to the involvement of the conus, but they were the result of tabes, that is, a posterior root lesion. The presence of the knee jerk

was due to intactness of the lumbar portion of the spinal cord, which is the seat of that reflex. In short, the clinical picture as represented by the patient, which was that of a pure conus lesion, could very well be explained by the tabes which he actually had been suffering from for seven years or more. Hence it follows that in some cases of conus lesion when the usual etiologic factors, such as traumas of the vertebral column, hemorrhages of the spinal cord, meningomyelitis, tumors, etc., can be excluded, tabes should be borne in mind as the possible actual disease.

**SYPHILIS IN ITS RELATION TO FEEBLE-MINDEDNESS.**—F. Kuhlmann, St. Peter, Minnesota. *The Journal-Lancet*, 1918, vol. xxxviii, p. 218.

The percentage of feeble-minded of all ages that give positive Wassermann reactions has been found in different groups to range from 1.5 per cent to 30 per cent. To interpret the meaning of these figures one must consider the following facts: The question as to whether a Wassermann reaction is to be called positive is in some measure a matter of judgment on the part of the observer. Positive reactions tend to disappear as the patients grow older. In a considerable percentage of syphilitic feeble-minded the disease is acquired, and stands in no causal relation to feeble-mindedness. The death rate among syphilitic children is exceedingly high, decreasing to a very large extent the number of syphilitic feeble-minded that might otherwise exist. In a considerable percentage of syphilitic persons when the disease is in the latent stage the Wassermann tests fail to give positive reactions. The syphilitic feeble-minded may, and in the majority of cases undoubtedly do, owe their mental deficiency to hereditary and other causes present at the same time, rather than to the syphilis. The frequency of syphilis in the general population seems to run nearly as high as it does in the feeble-minded.

**RELATION OF CONGENITAL SYPHILIS TO MENTAL DEFICIENCY.**—William H. Higgins, Richmond, Va. *The American Journal of Medical Sciences*, 1918, vol. clv, p. 551.

The object of this paper is to report the results of the serologic studies on the first 50 cases admitted to the psychologic clinic of the Medical College of Virginia during the past year. The material for this clinic is drawn largely from the retarded classes of the Richmond public schools, the juvenile court, and other agencies interested in the social welfare of the city. They were sent for the purpose of obtaining the estimate of their mental development as well as a clue to any factors influencing their mental moral stamina. In addition to the usual physical and neurologic examination, various psychologic tests were employed, the results of which are obviously unnecessary in this review. In this series 21, or 42 per cent, gave a positive Wasser-

mann reaction. Their ages varied from seven to sixteen years, and with the exception of one all were white. With two exceptions the general health of the children was uniformly good, a fact which made it difficult for the authors to impress upon the families the necessity for persistent treatment.

THE DIRECT AND DIFFERENTIAL DIAGNOSIS OF SOME OF THE COMMONER SYPHILIDES.—B. Barker Beeson, Chicago. *The Archives of Diagnosis*, October, 1917.

The earliest of the secondary syphilides is the roseola, erythematous syphilide, macular syphiloderm or syphilitic explosion. As a rule, it is first seen about 45 days after the appearance of the initial lesion. The roseola appears first on the lateral aspects of the chest and flanks, beneath the scapulæ and on the anterior surfaces of the forearms. It is composed of macular lesions which are circular or oval in contour and vary from 2 to 10 millimeters as regards diameter, the average being 4 to 6 millimeters. They are of a pale rose color, hence their name. They are nonelevated, do not scale, and give rise to no subjective symptoms. The luetic roseola does not reach its maximum development until about a week after its appearance. Papular syphilides are the most important group of syphilides, not only on account of their numerous varieties, but also because of their frequency and diagnostic value. Papules occur in what is known as the secondary period. They may be concomitant with the roseola, appear soon afterward, or be delayed until several years later. The lenticular papule will be taken as the type for this group, since a resumé of its characteristic when slightly modified will likewise serve for the other luetic papules. An orbicular configuration, a dark red, raw ham, or copper color, and marked infiltration are the characteristic attributes of such a papule. Three to five millimeters is the average diameter of these lesions and they attain an elevation from one-half to one millimeter above the adjacent skin surface. The title "nodular syphilides" has been chosen for this class of lesions in preference to that of "tubercular syphilides," which could easily lead to confusion with tuberculosis. They differ from papules in being larger, more indurated, more globular as regards form, and they penetrate more deeply into the derma. Furthermore, they are of a dark red or ham color, circular in contour, split-pea to large-bean sized and often later on they are covered by crusts. Nodular syphilides are especially prone to arrange themselves so as to form circles, arcs of circles, crescents, half-moons, etc. They occur late in the secondary or early in the tertiary period and are apt to be asymmetric and localized as a rule to a certain portion of the body, as on the face, especially over the nose, forehead, and on the shoulders. Gummata are late manifestations of lues and occur most frequently from the third to the sixth year after infection, although they have been observed forty to fifty years thereafter. They have

four stages—(1) development, (2) softening, (3) ulceration and (4) cicatrization. The lower limbs (42 per cent of all gummata), arms, and head are the common sites for these lesions. Often there is only a single gumma, but at times a number are present in a given area.

**STAINING FOR THE SPIROCHÆTA PALLIDA IN SMEAR PREPARATIONS.—**

Leon S. Medalia, Waco, Texas. *The Journal of the American Medical Association*, 1918, vol. lxx, p. 914.

The surface of the lesion is cleaned with a wad of sterile absorbent cotton, soaked in sterile saline solution, and all of the dried exudate is removed. The patient is then told to squeeze the lesion between the forefinger and the thumb until serous exudate appears. The appearance of the exudate may be hastened by scraping the deeper parts or the ragged edges of the lesion with a broken wooden applicator or with a stiff platinum wire. The exudate thus obtained from the deeper parts of the lesion should be mostly a serous exudate; real bleeding should be avoided. A good smear is one in which only an occasional red blood cell is found. The smears can be made on clean slides by placing a drop of deep exudate, obtained with a broken applicator, a sterile toothpick or a platinum loop, on one slide and spreading it out thinly with the other slide. The slides should not be pulled, but slid apart. The smears are then dried in the air, and stained with Wright's blood stain in the ordinary way, except that instead of plain distilled water to dilute the stain, 1 per cent solution of sodium carbonate in distilled water is employed. The film is covered with Wright's blood stain, to fix the smear, a sufficient quantity being used, a little in excess of what is used in staining blood smears. At the end of from one to two minutes, to the staining fluid are added from 45 to 50 drops of 1 per cent sodium carbonate solution in distilled water to a slide, or as much as the film will hold without running over. The diluted stain is allowed to remain on the film for fifteen or twenty minutes, and is gently steamed all the while with the flame of an alcohol lamp, as in the staining of sputum for tubercle bacilli by carbol fuchsin. The slide is then lightly washed with water, dried between filter paper, and examined with the oil immersion lens. The spirochetes appear intensely violet on a pale blue background, and are easily found.

**DEMONSTRATION OF THE SPIROCHÆTA PALLIDA BY LYMPH NODE PUNCTURE.—**Pontoppidan, Copenhagen. *Hospitalstidende*, 1917, vol. lx, p. 1227.

From December, 1916, to May, 1917, the author investigated 122 cases of untreated recent syphilis as follows: he punctured the largest inguinal gland with the needle of a Record syringe provided with a cannula which was held in place by two fingers of the left hand while



aspiration was practiced. Of 117 cases available for analysis, 58 were in males and 59 in females. The former presented 28 positive and 30 negative results, while the latter gave but 12 positive and 47 negative. Of interest is the fact that in 5 cases of positive find the Wassermann had not yet become positive. Other figures seemed to show that in the larger nodes (hazelnut or larger) the percentage of positive finds was highest, although to offset this the pea-sized nodes gave a larger percentage than the bean-sized ones. The sexual differences in the results can be explained on anatomic grounds, for in some of the women the deeper seat of the primary lesion would tend to involve the pelvic lymph nodes at the expense of the inguinal glands.

**STUDIES ON IMMUNITY WITH SPECIAL REFERENCE TO COMPLEMENT FIXATION.**—Alfred Blumberg, Salt Lake City, Utah. *The Journal of Laboratory and Clinical Medicine*, 1918, vol. iii, p. 408.

The author has shown that true antigens (e.g., antigens that contain the etiologic factor of the disease, emulsified or autolyzed) will work only where there is a polymorphonuclear leucocytosis present. While tuberculosis is a disease presenting a lymphocytosis, it will fix the complement with a specific antigen, which, however, is not a bacterial emulsion, but a heated egg medium culture containing small amounts of lipid. Tissue extracts of mammals, birds, reptiles and fishes may serve as useful antigens for the diagnosis of syphilis. If normal urine is added, the complement of the hemolytic system is affected without the presence of a specific antigen. The presence of hemolysis in the test of the fourth group indicates either some type of affection of the kidney (even when no albumin or casts are demonstrable) or pregnancy, the two conditions frequently being separable by the clinical history of the patient. The absence of hemolysis in a hemolytic system to which urine is added speaks against the condition of pregnancy. In complement fixation without antigen, reaction affecting the third tube (which serves as a control tube and should not hemolyze) speaks for nephritis rather than pregnancy.

**REPORT OF THE COMMITTEE ON UNIFORMITY OF THE WASSERMANN REACTION.**—William Litterer, Nashville, Tenn., and Chas. Waterson, Birmingham, Ala. *Southern Medical Journal*, 1918, vol. xi, p. 267.

A uniform technic and a uniform antigen in the hands of men trained in laboratory work will give uniform results if adhered to closely in every detail. Before the results obtained with the Wassermann test are uniform, a method of standardizing the antigen must be found and the men performing the test must agree as to technic.

A NEW METHOD OF PRESERVING AND MAILING SPECIMENS FOR A WASSERMANN.—W. L. Snider, Hot Springs, Arkansas. *New York Medical Journal*, 1918, vol. cvii, p. 831.

This method is especially applicable in cases in which the specimen must be sent some distance to the laboratory. It consists of applying a small square of cantharidal blister plaster to a convenient point on the skin; removing it in about two hours; placing over this point a vaccination shield; and the next morning puncturing the blister with a needle and collecting the serum on special blotting paper. The serum is allowed to dry and the paper is then enclosed in an envelope and mailed to the laboratory. The advantages are simplicity in collecting material, convenience in mailing, and the keeping property of the serum in a dry state. Venipuncture is rather an easy operation when one has the proper needle and much practice, but with a dull needle and the amount of experience in this line that most physicians in general practice have, it is usually very exasperating for the doctor and a very painful ordeal for the patient. The blister method is obviously simple and is painless to the patient. When blood is used as material upon which the Wassermann is done one has to be extremely careful in having the container sterile and the blood must be kept on ice to prevent bacterial growth. If bacterial growth occurs it changes the blood and its serum so that it is impossible to carry out a reliable Wassermann test upon it. It is, therefore, impracticable to send blood to a laboratory if it will have to be on the way a long time. The serum dried on paper will retain its power to produce a Wassermann reaction for ten days or more and, being in a dry state, is not affected by bacterial growth. Another advantage of this method is that the laity are not familiar with it, while the blood test and what it is for is known by a great many people. When we ask a patient, especially a woman, to allow us to make a blood test, the chances are that we will offend her or some of her family, for they know at once that syphilis is suspected. It is essential, however, that syphilis be ruled out of many of the chronic cases one is called upon to treat.

PRESENT STATUS OF DIAGNOSIS AND TREATMENT OF SYPHILIS.—W. P. Garshwiler, and John R. Thrasher, Indianapolis, Ind. *Mississippi Valley Medical Journal*, 1918, vol. xxv, p. 169.

Two sores may appear at the same time, one chancreoid from the last intercourse of a few days before, and the other luetic from an exposure two or three weeks before. The Wassermann test becomes positive in fifty per cent of cases in fourteen days after the appearance of the chancre. This percentage rapidly increases in the succeeding weeks and is almost uniformly constant during the second period. Occasionally it is plus in forty-eight hours, and again very rarely it may not become plus in three or four months. In the secondary stage

the dark-field has a much broader field of application, on account of the multiplication and wider distribution of the organisms. Spirochetes may be found here in the induration of the healed chancre, in the skin lesions, in any large lymph gland, in the tonsils, whether mouth lesions are present or absent, in mucous patches of mouth, anus and genitals and in condylomata. The dark field and the Wassermann will frequently detect at once what might otherwise require weeks or months to determine. The authors think the general practitioner who uses the Wassermann should be very careful in giving weight to any examination under three-plus or 75 per cent. They think this limit reasonably safe. Where it is less than that, the general practitioner had better disregard this evidence in making his diagnosis. On the other hand, the man who for years has used the Wassermann in close clinical association can carry his examination down almost to zero. To him a Wassermann examination means the serologic readings of the blood over a certain period of time. It means also the influence of provocative salvarsan, or provocative iodides on a series of readings. It means also the effect of intensive treatment over a certain period of time on the findings—a slowly diminishing serologic reading being just as much a therapeutic test as the rapidly disappearing clinical lesion under antisyphilitic treatment. It means also the complete serologic record of the blood and spinal fluid. Our spinal fluid record is not complete, however, unless it includes also cell count, globulin estimation and colloidal gold test. In early syphilis the authors give .15 salvarsan each three, seven and ten days apart, until the patient has had from fifteen to twenty doses. The Wassermann is taken each four weeks. After this first series, an injection of salicylate of mercury, one grain a week for six to fifteen weeks. By alternating these series of salvarsan and mercury injections we are generally able to force a 100 per cent down to negative, the intensity of the treatment being reduced with the reduction of the Wassermann. Treatment is continued for at least six months after the blood and spinal fluid become negative.

THE VALUE OF CHEMICAL TESTS ON THE SERUMS AND SPINAL FLUIDS OF SYPHILITICS.—Boris Mann and Anna I. van Saun, Albany, N. Y. *New York Medical Journal*, 1918, vol. cvii, p. 787.

Most of the chemical tests are nonspecific for syphilis. In general they show only a pathologic state. In the author's hands the mercuric chloride test with the blood serum of suspected syphilitics failed to correspond with the results obtained with the Wassermann test in more than half of the 248 specimens studied and thus lacks diagnostic value. With spinal fluids the mercuric chloride test indicates the presence of proteins, but beyond this it can not be considered specific.

SYPHILIS IN CHILDHOOD.—H. E. Michelson, Virginia, Minn. The *Journal-Lancet*, 1918, vol. xxxviii, p. 159.

The well-known symptoms are the following: Snuffles, that is, a coryza with its accompanying hoarse cry. This affection begins with the swelling of the nasal mucous membrane; later there is a serosanguineous discharge with crust-formation and subsequent ulceration, sometimes followed by perforation of the septum, and if the nasal bones are destroyed, the nose will fall down, leaving the characteristic pug- or saddle-nose. Optic neuritis, interstitial keratitis, and iritis are found with relative frequency. Sudden deafness, due to a specific neuritis of the auditory nerve, is also described. This may be the only symptom of syphilis noted in that individual. The typical convergent barrel-shaped, notched, upper central incisors, or Hutchinson teeth, although often described, are by no means a common accompaniment of syphilis. The glandular system is often involved, a general adenopathy is not rare, and the cubitals are usually palpable. The spleen and liver are often enlarged and hard, due to chronic diffuse interstitial change. Syphilomata of the liver and spleen are rare in congenital lues. Involvement of the urogenital system is also rare. Syphilitic pemphigus, when present, is a typical lesion. It is a bullous eruption, appearing first on the soles and palms, but later may invade other regions of the body. Mucous patches may develop about the mouth or anus; and radiating fissures and rhagades are often present, and are pathognomonic if they are definitely linear and not confined to the angles of the mouth. The papular, pustular, and ulcerating syphilides may all be present, and the desquamated, hypertrophied, papular eruptions, or condylomata, are often seen in any region where two opposing skin surfaces rub together, as in the circumanal or genitocrural regions. The roseola of acquired syphilis is never found in congenital syphilis. The favorite location of the maculopapular syphilides is the forehead and the hairy scalp. The lower extremities, the flexor surfaces of the upper extremities, the neck, chin, and face, and the palms and soles are all common seats of cutaneous manifestations, while the trunk is usually free from eruptions. The skin lesions of late hereditary syphilis differ in no way from those found in acquired syphilis. The Wassermann reaction is positive in practically 100 per cent of cases, in late childhood. The neosalvarsan had best be used because of the difficulty in keeping a child still long enough to inject salvarsan, which must be more diluted. After two years of age, the drug can be given intravenously in 5 c.c. of freshly distilled water, and may be repeated weekly until all clinical symptoms except the Wassermann reaction have disappeared. The use of mercury should always be combined with arsenic. Children stand mercury very well. The intramuscular injections are prohibited because of the delicacy of the tissues in children. The inunctions are well borne, especially after one year of age, 1 gm. of the 10 per cent

ointment being rubbed in daily. The ointment may be rubbed into the area and a flannel binder applied over the area rubbed. The iodides are not well borne by children. They are unnecessary in early infantile syphilis, and should be used only in late recurrences or where the absorption of a gumma is sought.

**THE VALUE OF THE WASSERMANN REACTION.**—John H. Larkin, I. J. Levy, John A. Fordyce, New York. *The Journal of the American Medical Association*, 1918, vol. lxx, p. 1594.

The term "Wassermann reaction" includes several methods of serologic procedure. An accurate interpretation of each method is essential in arriving at a proper diagnosis. A positive reaction is the most constant symptom of syphilis. The value of the reaction in diagnosing undoubted syphilis is shown by the fact that the reaction is positive in practically 100 per cent of the cases of florid syphilis. In active tertiary syphilis of the skin and bones the reaction is positive in about 94 per cent of the cases. In syphilis of the central nervous system, cognizance must be taken of the reaction in both blood and spinal fluid. The blood is positive in about 80 per cent of the cases. In a pathologic study, the Wassermann reaction (alcoholic antigen, warm fixation) was positive in 94 per cent of cases of syphilitic aortitis. As a means of corroborating syphilitic infection, the Wassermann test is at least 90 per cent dependable, as shown in a series of positive reactions in which 90 per cent could be accounted for by syphilitic changes in the aorta alone. The value of negative reaction has been studied and its reliability confirmed by the negative reactions obtained in non-syphilitic affections of the skin. In a series of necropsies in which it was demonstrated pathologically that the aorta was free from syphilitic disease negative reactions were obtained in 91 per cent.

**TITRATION OF COMPLEMENT FOR ITS POWER TO COMBINE IN THE SYPHILITIC SYSTEM.**—Arthur William Stillians. Chicago. *The Journal of Cutaneous Diseases*, 1918, vol. clv, p. 293.

The use of a mixture of glycerinized strong positive serums, titrated with each set of Wassermann tests as a positive control, gives an accurate idea of the strength of the Wassermann reaction. Titration of complement against the combination of antigen with a fraction of the titer of this positive control gives valuable information as to the combining power of the complement in the syphilitic system. By the use of this method of titration, variations in strength of the Wassermann reaction can be minimized. Old complement is apt to lose its power to combine in the syphilitic system before its hemolytic value fails. Such variations are detected and estimated by the new method of titration.

THE WASSERMANN REACTION: ITS USE AND ABUSE.—Hugh W. Bayley, London. *The Lancet*, 1918, vol. exciv, p. 632.

A symptom does not become useless for diagnosis because it is not pathognomonic, and it is the sum of various symptoms, none of which may be pathognomonic, that establishes diagnosis. The author considers the Wassermann reaction as one of the most valuable symptoms of syphilitic infection that we possess, but that diagnosis can not be based with certainty on this symptom alone, even if the reaction is strongly positive, and that weak positives are useless for diagnosis. A negative Wassermann is of especial value when lesions of a doubtful nature are present and render it highly improbable that syphilis is the cause of the lesions. A negative Wassermann of the cerebro-spinal fluid is probably sufficient evidence to exclude G. P. I. A negative reaction also indicates that the treatment given has been efficient, but one or two negatives are no proof of permanency of cure.

SOME IMPORTANT PRINCIPLES WHICH DETERMINE THE RELIABILITY OF THE WASSERMANN REACTION.—James McIntosh, London. *The Lancet*, 1918, vol. exciv, p. 630.

In spite of the many inherent difficulties of the Wassermann test, discordant results can be greatly reduced, if not entirely abolished, by the adoption of a method which standardizes all the reagents used in the test. By the adoption of such a technic that bogey known to all who perform the test as a "bad day" will be entirely eliminated, and the performance of the test becomes almost mechanical, since nothing is left to chance. The secret of this lies not in the adoption of a certain technic, but in the recognition and practice of certain important principles. The actual technic by which these principles are put into operation is of secondary importance. These principles are: (1) Adoption of a constant antigen, (2) titration of complement in the presence of the antigen, (3) employment of 4 to 6 units of a high-titer amboceptor, (4) inactivation of the sera to be tested for half an hour at 55° C. The technic by which the Wassermann reaction is carried out is unimportant, provided it is exact and embodies the above-mentioned principles.

THE CAUSE OF LUMBAR PUNCTURE HEADACHE.—Russell G. MacRobert, New York. *The Journal of the American Medical Association*, 1918, vol. lxx, p. 1350.

Lumbar puncture headache differs from all others in that, being present when the patient is sitting up, it completely disappears when he lies down. It is throbbing and severe, and felt mostly in the frontal and occipital regions. No drugs give sufficient relief to allow its victim to walk about and attend to his affairs, or even to sit up. The pain comes on quickly when he sits up, being fully present in twenty

seconds. It takes about the same length of time to subside when he lies down. This situation usually persists for about seven days with full severity, and then ends somewhat abruptly in the course of twenty-four hours. The only effective treatment is a week's stay in bed with the head low. While in this position the patient is quite comfortable, and there are no clinical signs of trouble present. Regarding causative or influencing factors of the headache, various speculations have been made concerning the importance of such points as the rapidity with which the fluid is withdrawn; the position of the patient during the puncture; the degree of pressure existing in the spinal fluid at the time of puncture; the disease condition of the patient, and his age. All these points are now generally regarded as unimportant. If the puncture hole is not blocked, it is because the delicate arachnoid tissue clings around the departing needle, and its hole is pulled into and through the hole in the dura. There it impinges, and this invagination forms a spout or wick for the easy drainage of the whole cerebrospinal fluid sac, and also prevents the rapid healing, which would otherwise occur, of so small a dural opening. All the fluid secreted by the choroidal glands during seven or eight days, the time seemingly necessary for the hole to close by tissue growth, will be lost by leakage into the epidural space, where it can be absorbed readily, because the epidural space of the spinal canal is comparatively very large, and contains only loose connective tissue, with venous plexus and lymph channels. It is evident, in the light of the foregoing facts, that the amount of fluid collected in the test tube will be no indication whatever of the great loss that occurs, when a puncture hole does not become properly occluded when the needle is withdrawn.

THE PREPARATION OF COLLOIDAL GOLD.—Frederick G. Speidel, and J. W. Smith, United States Naval Reserve Force. United States Naval Medical Bulletin, 1918, vol. xii, p. 224.

Place 1,000 c.c. of triply distilled water in a 2-liter Erlenmeyer flask. (A large flask facilitates vigorous agitation at the end of the procedure.) Add 10 c.c. of 1 per cent gold chloride solution and 7 c.c. of 2 per cent potassium carbonate solution. Place over a Bunsen burner and heat rapidly to boiling. When the boiling point is reached, as evidenced by the rising of bubbles, remove from the flame and with constant agitation add 4 c.c. of 1 per cent formaldehyde (2.5 per cent formalin) solution. Continue to agitate vigorously and the solution will be seen to assume a faint bluish tinge and pass rapidly through a deep amethyst to a beautiful red color, which indicates that reduction is complete. This is the final product, and it should conform to the following requirements: (1) The solution must be absolutely transparent and preferably of a brilliant red-orange or salmon-red color. (2) Five c.c. of the solution must be completely

precipitated by 1.7 c.c. of a 1 per cent solution of sodium chloride in the time interval of one hour. (3) The solution must be neutral in reaction. (4) It must give a typical reaction with a known paretic cerebrospinal fluid. (5) It must produce no reaction greater than a No. 1 with known normal cerebrospinal fluid. If a solution results that is unsatisfactory in any of these particulars, it should be discarded, and, after a careful and thorough recleaning of all glassware, another solution made up. This procedure has always resulted in a satisfactory solution and takes less time and is less trouble than trying to "correct" a poor solution.

THE COLLOIDAL GOLD (LANGE) TEST IN DIAGNOSIS.—Richard W. Harvey, San Francisco. *California State Journal of Medicine*, 1918, vol. xvi, p. 173.

Observations on this series support the opinion of previous workers, that while the colloidal gold test is valuable, it does not replace other tests but confirms them and in some instances assists in a prognosis. The test is valueless unless a satisfactory indicator is prepared. It is simple of execution, and the error is small if the precaution is observed of obtaining blood-free spinal fluid in clean, sterile tubes. In congenital lues the reaction does not add to the evidence given by other spinal fluid tests, but it is of confirmatory value. In tabes the test, besides confirming evidence from other sources, may, when it gives a paretic curve, predict the development of a paresis. In tabes and cerebrospinal lues it may be positive in cases in which the Wassermann, cell count, and globulin are negative. In general paresis it is invariably positive and is of absolute value in differentiating between general paresis on the one hand and tabes and cerebrospinal lues on the other. In normal fluids it is invariably negative if Miller's rule of counting all color changes below 2 as negative, is followed. Where the laboratory facilities are such that care and time may be devoted to the preparation of a suitable indicator the test should be performed on every spinal fluid; the data or diagnosis is incomplete otherwise.

PERMANGANATE REDUCTION INDEX OF CEREBROSPINAL FLUID.—Ernst Albrecht Victors, San Francisco. *California State Journal of Medicine*, 1918, vol. xvi, p. 175.

The field for the application of the reduction index appears to be limited to young children evidencing symptoms of meningeal irritation, and is of differential aid in determining a true involvement of the meninges and diseases other than meningitis but which appear meningeal. The inconstancy of cytologic findings and the difficulty of demonstrating causative microorganisms in these borderline conditions, gives to this test a certain sphere of usefulness. The reduc-



tion index is usually below 2 with normal fluids and the upper limit of normal fluids as determined by Mayerhofer is 2.3 and by Hoffman and Schwartz as 2.5. In tuberculous meningitis there is a constantly high index, especially in the last portion of the fluid. In serous meningitis, on the other hand, the index is relatively lower and higher in the first portion.

THE PROBLEM OF VENEREAL DISEASE IN ITS RELATION TO PENAL INSTITUTIONS.—Edith R. Spaulding, Bedford Hills, New York. *Medical Record*, 1918, vol. xciii. p. 717.

The author believes that wherever a physical examination is necessary in the case of individuals passing through our courts it should include laboratory tests for gonorrhea and for syphilis. A physical examination is necessary in every case which is under the care of the State for any period of time, whether it is in a penal institution, an industrial school, or a jail. All cases found to be positive should receive treatment. There is in Massachusetts a law, which also exists in Connecticut, that states that inmates of public, charitable or penal institutions shall be held for treatment of syphilis while the disease is in a communicable form. This law is of great benefit in bringing extra pressure to bear in forcing any uncooperative individuals to receive treatment. Provision should be made in the community for hospital treatment of venereal disease to encourage care of such infections in their earliest stages and for follow-up work of those cases whose treatment has been begun in institutions. We should not forget that the question of mental defect in the community is closely associated with that of venereal disease, as well as with delinquency. When we realize the real need of segregating the feeble-minded and are able to care permanently for this class of social inefficients, we shall remove a great source of infectious disease from the community. Twenty-three per cent of the women at the Reformatory at Framingham who were fit subjects for permanent segregation on account of their mental defect, showed 90 per cent of gonorrhea and over 60 per cent of syphilis. It is believed by authorities both in Europe and in America that before the war is over the need will be recognized for a law requiring the notification of these diseases which will place them on an equal footing with other contagious diseases, will make treatment compulsory, and will tend to lessen the danger of further infection. At some future date when our probation and parole departments have adequate medical equipment, and there is more emphasis laid on therapeutics in the treatment of delinquency, examination may be made also of the families of delinquents. At the Boston Psychopathic Hospital an effort is made to bring to the hospital for examination the wife or husband of every syphilitic patient treated and the members of the patient's family under eighteen years of age.

## SYPHILIS IN ITS MEDICAL, ITS GENERAL, AND ITS SOCIOLOGICAL ASPECTS.

—L. G. Rowntree, Minneapolis, Minn. *The Journal-Lancet*, 1918, vol. xxxviii, p. 224.

There are two great problems facing anyone attempting to interest the State in the treatment of syphilis in the early stages. The first is the need of statistics. Syphilis is a secret disease. A great many individuals take no treatment; and a great many take treatment for an insufficient period of time, and then disappear from sight. The latent period of syphilis is reached, and treatment is not considered necessary until parasymphilitic diseases develop later in life. It is not a reportable disease, although it is an infectious disease. We have practically no data. If the Safety Commission or any other intelligent body is approached for funds for the fight against syphilis, the question is immediately asked, "What is the prevalence of syphilis?" Nobody knows. "Is there any possibility of getting at it?" Not with accuracy at the present time. One can, of course, get certain ideas, surveys, and estimates. For instance, more than 13 per cent of the patients admitted to the University Hospital in the last six months have had syphilis, and up to 5 per cent more are not above suspicion. A small survey was made in the Peter Brent Brigham Hospital in Boston. Of the 4,000 patients admitted, 15 per cent had positive Wassermann evidence of either active or latent syphilis.

SOME SUGGESTIONS FOR THE COMMUNITY CONTROL OF VENEREAL DISEASES.—J. W. Kerr, Washington, D. C. *Social Hygiene*, 1918, vol. iv, p. 80.

Aside from special means, the following general preventive measures among civilians for the protection of the military forces would appear to be possible: 1. Education by means of publications, lectures, and conferences properly used. 2. Prohibition of prostitution within specified areas. 3. Prohibition of street-walking. 4. Exclusion of the residence of prostitutes within certain areas of cities. 5. Abolition of all signs indicating red light districts and the thorough policing of suspected areas. 6. Prompt arrest of intoxicated persons in such districts. 7. Prohibition of sale or consumption of liquors in disreputable resorts. 8. Opening of hospitals to cases of venereal diseases as to other communicable diseases.

HAVE WE DEVISED AN EFFECTIVE MEDICAL PROPAGANDA OF VENEREAL PROPHYLAXIS?—R. C. Holcomb, United States Navy. *Social Hygiene*, 1918, vol. iv, p. 69.

Education by means of the navy leaflet should be continued and the instruction contained therein should be amplified by talks by the medical officer as has been practiced for several years, and is still

in practice. The pamphlet may well be assisted by use of posters and dialogues with a moral. Medical prophylaxis has not yet given the results that were expected of it in the navy, and its value diminishes rapidly with the length of time since exposure. Medical prophylaxis may give a false sense of security, thus actually doing harm, and care should be taken to see that men do not receive the suggestion that by this means an infallible protective is offered. Station prophylaxis should be given as long as there is any chance that it will reduce the incidence of venereal disease. Medical officers, chaplains and line officers should teach the value of chastity in preventing these diseases, and should encourage a variety of athletics in which all men may participate instead of a selected few on teams or in boats' crews. Foreign duty increases the incidence of venereal disease. All night liberty for a minor in training is to be avoided. He would be in better shape for duty the next day and it would be better for him if the officers gave him all day liberty. Stoppage of pay has not been in practice in the navy long enough to learn what effect it may have on incidence, and damage due to venereal disease. Men who are infected should, during the acute stage of disease, be quarantined to their ship or station, a practice long enough in vogue in the navy. Men with disease should be given printed pamphlets concerning their trouble, telling them how to care for themselves and how to protect others. Since men with syphilis can not be quarantined for all treatment and observation necessary, and as they are subject to transfer from duty to duty, a signal sheet should be used which will at once attract the attention of the medical officer, and which will give him a concise abstract of the man's history including serologic tests, amount and frequency of salvarsan and other treatment, and all facts necessary to give the man the best chance for ultimate cure. This is the practice in the navy.

GLOBULES OF METALLIC MERCURY IN THE TISSUES.—John A. Kolmer and E. V. Mastin, Philadelphia. *Journal of the American Medical Association*, 1918, vol. lxx, p. 1291.

While mercury has an apparent protoplasmic affinity for the *Spirochete pallida*, explaining the specificity of the drug in the treatment of syphilis, the deposition of mercury in the tissues bears no relation to the distribution of spirochetes; the authors were unable to find spirochetes in the eroding mercury-laden aneurysm, and numerous chemical studies have shown the presence of mercury in the liver and other internal organs of otherwise normal experimental animals, also in healthy rabbits following inunctions of mercurial and calomel ointments. So far as the deposition of metallic mercury is concerned, it would appear that this occurs by reason of chemical changes in necrotic tissues of syphilitic or nonsyphilitic etiology.

THE INTRAVENOUS USE OF RED MERCURIC IODIDE.—L. W. Rowe, Detroit, Michigan. *The Journal of Laboratory and Clinical Medicine*, 1918, vol. iii, p. 415.

Red mercuric iodide in combination with an equal amount of potassium iodide can be injected in solution into animals intravenously with comparative safety if reasonable care is exercised in the manner of injection and in the size of the dose injected. It is very little if any more toxic than mercuric chloride, safer for intravenous use, and because of its greater germicidal efficiency should be found to be of therapeutic value.

TREATMENT OF RECENT SYPHILIS.—Gaucher, Paris. *Annales des maladies veneriennes*, 1918, vol. xiii, p. 65.

The late distinguished successor of Fournier, as head of French syphilography and a notable foe of salvarsan, formulated the treatment of recent syphilis as follows, not long before his death. Mercury, the remedy to use, whatever its form of exhibition, must be soluble and absorbable. If one gives pills they should be of sublimate; if a solution, Van Swieten's liquor or mercuric lactate, 1:1000. If the hypodermic route is preferred, the solution of biniodide or benzoate, 1:100. The injections should always be made in the buttock. If one must use the intravenous route, which is seldom required, the cyanate is the salt of preference. An exception to the author's rule of solubility is the inunction of blue ointment in which the active remedy is minute quantities of mercury vapor. The dosage and plan of treatment comprise nothing especially new. The iodides, sulphur, organic arsenicals (not salvarsan) are useful only as auxiliaries.

TOXICITY OF THE AMERICAN-MADE ARSPHENAMIN (SALVARSAN).—James C. Sargent, Milwaukee. *Journal of the American Medical Association*, 1918, vol. lxx, p. 908.

Three ampules, each containing 0.6 gm. of arspenamin, were inspected and found not to be cracked. The contents of each was of the characteristic pale yellow color. The total of these ampules was dissolved in 225 c.c. of sterile water which had been distilled less than two hours before. After the arspenamin was entirely dissolved, the solution was alkalized by the addition of a sufficient quantity of 15 per cent sodium hydroxide to form and redissolve the precipitate. It might be said that this technic, together with that of the injection of the solution, was identical with that used in the administration of some 200 doses of salvarsan given in the past six months. Having been convinced that these five cases alone were sufficient to give a very definite idea of the toxicity of the new American-made salvarsan (arsphenamin) the author has abandoned its use.

REPORT ON ARSPHENAMIN.—Victor N. Meddis, and William C. Stirling, Louisville, Ky. *Journal of the American Medical Association*, 1918, vol. lxx, p. 1459.

The arsenobenzol brand of arspenamin made in this country is in the authors' experience nontoxic, and equally as efficient therapeutically as the original Ehrlich preparation. It may be used in concentrated solution with no ill effects. Epinephrine, given in a 1:1000 solution ten minutes before the injection, will control reaction. The only reaction noted in this series of cases was slight headaches; in some cases, diarrhea and slight malaise were noted. In phagedenic chaneroids, "arsenobenzol" has a very beneficial effect, and is recommended where the healing is slow and response to other treatment is poor.

THE TREATMENT OF SYPHILIS.—Harrison, Rochester Row, London. *The Dublin Journal of Medical Science*, 1918, vol. cxlv, p. 283.

Salvarsan, or any of its equivalents, is used as follows: Seven weekly doses of "606" intravenously, commencing with 0.3 gram for the first 3 doses, followed by 3 doses of 0.4 gram, and finishing up with one dose of 0.5, a total dosage of 2.6 grams being given. If administered intramuscularly, two .45 doses, followed by five .6 grams, a total of 3.9 grams being given. With each dose a weekly dose of 1 grain of Hg is given intramuscularly in the form of mercurial cream. If at the end of the course the patient's blood gives a negative Wassermann, he is let alone, and directed to have a blood test at the end of 2, 4, 6, and 12 months. This is an important result of treatment by newer drugs owing to the absence of any lowering of vitality. Soldiers were quite fit to return to duty at once without any convalescence; in fact, were usually much improved in general health. If however, the blood is positive or doubtful, he is put on a course of iodide of potassium for 14 days and at the end of that time receives further two weekly doses of 0.3 and 0.4 gram of "606" and 1 gr. Hg. Tertiary cases receive the same course, which is repeated after intervals, during which KI and Hg are administered. Each case must be treated on its merits, and one is guided by the repeated Wassermann results. In spite of many such courses there are a number of late cases of syphilis which will never give a negative Wassermann. Regarding the question of cure, all active signs having disappeared, and repeated Wassermann examinations proving negative at intervals of every three months during the first year and six during the second, the examination before the late tests being preceded by the administration of a provocative dose of "606," and, in addition, the cerebrospinal fluid proving negative, the author thinks one could reasonably give the patient a clean bill of health.

## BOOK NOTICES

(Books for review should be sent to Dr. W. H. Deaderick, Associate Editor,  
Dugan-Stuart Bldg., Hot Springs, Arkansas.)

**LOCOMOTOR ATAXIA.**—By Wm. J. M. A. Maloney, M.D., Fellow of Royal Society of Edinburgh, Fellow of New York Academy of Medicine, Fellow of New York Neurological Society, Neurologist to the Central and Neurological Hospital, Former Professor of Neurology, Fordham University. 299 pages. Illustrated. New York, D. Appleton & Company, 1918.

The author begins by consideration of the spirochete, as the cause of tabes. Pathology and pathogenesis are carefully detailed throughout several chapters. The chapter on diagnosis is particularly interesting. The author is somewhat therapeutically nihilistic as to the medicinal treatment of tabes and as to intensive treatment of syphilis preventing tabes. He states that as tabes does not necessarily follow untreated or cursorily treated syphilis, as tabes may occur in spite of intensive antisymphilitic treatment and as antisymphilitic treatment may not lengthen, and may even be associated with a shortening of the pretabetic period, the value of antisymphilitic treatment in preventing tabes needs proof. We can not by metallic substances alone surely kill the invading spirochete. Modern therapy pays too much attention to the spirochete and too little to its host. The Maloney method of treatment is directed chiefly toward the host. One of the greatest clinicians has said, "Know syphilis in all its manifestations and relations and all other things clinical will be added unto you." It might be added, know tabes and you will know syphilis. The author's style is excellent and his clinical descriptions extremely clear. This book should be of utmost interest to the neurologist and syphilologist.

**THE THIRD GREAT PLAGUE.**—A Discussion for Everyday People.—By John H. Stokes, A.B., M.D., Chief of the Section of Dermatology and Syphilology, the Mayo Clinic, Rochester, Minn. 12mo of 204 pages. Cloth, \$1.50 Net. Philadelphia and London: W. B. Saunders Company, 1917.

Ordinarily a little knowledge is a dangerous thing, particularly in medicine. This is especially true when the layman attempts to obtain information from medical books. The present work, however, is written for laymen and conveys a great deal of knowledge about a very complex subject. As the author states, the simple device of talking plain matter-of-fact English about a thing, has a value that we are going to appreciate more and more every day and that nothing in

the past has done so much in the campaign against consumption as the unloosening of tongues. The same is true of syphilis. Syphilis is regarded as a problem of public health rather than of morals. He estimates that one man in ten has syphilis; and that the proportion of syphilitics who develop the late nervous manifestations probably does not greatly exceed 1 per cent. The interpretation of the Wassermann test is given clearly and sanely. Stokes believes the test should be made by specialists of recognized standing, that this term does not include many of the commercial laboratories which spring up like mushrooms in these days of laboratory methods and that the results should be interpreted to the patient by the physician and not by the laboratory that does the testing or in the patient's own half-knowledge of the matter. Speaking of the discovery of salvarsan, he says there could be no better example of the employment of animal experiments in medicine. The dangers of salvarsan are easily exaggerated and some people bear a foolish fear of it. There is every reason to believe that radical cure under the newer methods is a practical and attainable ideal in a high percentage of cases and offers all the assurance that any reasonable person need ask for the conduct of life. The author thinks that the system of making syphilis a reportable disease may finally be placed in the category of premature legislative experiments, and should be postponed until a more favorable time. The style of the book is clear and the makeup of the usual Saunders type. Every physician should see that this work is in the hands of each of his syphilitic patients.

**THE INTENSIVE TREATMENT OF SYPHILIS AND LOCOMOTOR ATAXIA BY AACHEN METHODS.**—By Reginald Hays, M.R.C.S., with a Preface by M. A. Bliss, Washington University Medical School. 88 pages. Illustrated. Price \$1.50. St. Louis, C. V. Mosby Company, Publisher. 1917.

By Aachen methods the author means the inunction of a 33 $\frac{1}{3}$  per cent mercurial ointment by the bare hands of a skilled rubber under proper medical supervision and in addition the use of sulphur water internally and externally as administered at Aachen. The author endeavors to show that this method if properly applied yields better results than are obtained by any other mode of giving the drug and this without danger or pain. Unskilled or haphazard methods of application lead to uncertain results, which is undoubtedly responsible for the fact that in the country, excepting in certain health resorts, inunction does not today hold the position to which it is justly entitled. The various methods of administration of mercury are considered in detail. The author is a warm advocate of the inunction method if applied in properly selected places by a skilled rubber which he considers a very essential point, and controlled by careful supervision, claims for the method safety, potency, and painlessness

with exemption from most of the drawbacks which are seen to attend other kinds of treatment. It is this method that has made certain spas of Europe and America famous. The length of treatment generally considered necessary in a case of uncomplicated syphilis during the first two years, has until lately been about six months taken in courses of four to six weeks with intervals of rest. Many authorities, however, dissatisfied with results so obtained and as an outcome of their practical experience have regarded with favor a further short course yearly for three or four years or possibly longer even in the absence of clinical manifestations. To the text is appended a series of illustrative cases. The inunction method in the treatment of syphilis has proved very effective when properly administered. Those wishing to familiarize themselves with the details of this method will find this little monograph indispensable.

**SYPHILIS AND PUBLIC HEALTH.**—By Edward B. Vedder, A.M., M.D., Lieutenant-Colonel, Medical Corps, United States Army. Published by Permission of the Surgeon-General United States Army. 315 pages. Cloth, \$2.25. Philadelphia and New York. Lea and Febiger, 1918.

In an introduction the author considers the importance of syphilis in relation to public health. The four chapters of the body of the work treat of the prevalence of syphilis, the sources of infection and methods of transmission, personal prophylaxis and public health measures. In the appendix is included an excellent account of the technic of the Wassermann reaction and various regulations of cities, states and the army for the control of syphilis. The author thinks that it is conservative to estimate that from 10 to 20 per cent of private patients are infected with syphilis. He concludes that syphilitic infection may usually be prevented by means of the prophylactic ointment if it is applied reasonably early after exposure. In regard to syphilis and marriage Vedder accepts the following standard of cure: One year without treatment, without any suspicious clinical signs, with several negative Wassermann reactions and no positive ones and with a negative provocative Wassermann reaction and luetin test at the end of the year. He believes that sex education should be supplied by parents and that such instruction has no place in schools below the rank of colleges. He affirms that we are logically driven to accept systematic treatment as the only method left to the community to reduce the number of venereal infections, particularly syphilis. With reference to reporting cases of syphilis, the author urges that the real objections that must be met are that this will turn these cases over to quacks and charlatans, that it must be made a benefit to patients as well as to the community and that ample facilities for treatment for all classes of patients must be first provided. The work is invaluable to practitioners, social workers and health officers.



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## Original Articles

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### ON SYPHILIS OF THE NERVOUS SYSTEM

PATHOLOGICAL, SEROBIOLOGICAL AND CLINICAL CRITERIA WITH ESPECIAL  
REFERENCE TO TREATMENT

BY DAVID J. KALISKI, M.D., AND ISRAEL STRAUSS, M.D.

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(Received for publication, September 2, 1918)

**I**N a previous communication we presented a summary of the results of treatment of more than one hundred and twenty cases of various types of syphilis of the nervous system. During the three years that have elapsed since that paper was presented we have had the opportunity of observing most of these patients. We have studied and treated during the past four years more than four hundred cases covering the entire field of syphilitic nervous diseases.

It is our purpose in this communication to outline the methods and rationale of our therapy. We shall point out that further experience and study have served to strengthen our belief in the efficacy of more persistent and intensive treatment not only in the earlier more readily curable or remediable forms of neurosyphilis, but also in the later and more chronic forms of the disease.

An intelligent approach to the treatment of syphilis of the nervous system necessitates a consideration of the pathologic processes which are present in this disease, with a view of explaining the possibility of influencing these lesions by therapy; and we shall endeavor to emphasize in our consideration of the subject the type of lesion in the light of our knowledge of the action of various therapeutic measures in influencing the disease.

In view of the many discoveries of the last decade, beginning with the discovery of the *Treponema pallidum* and of the Wassermann reaction of the blood and spinal fluid up to the time of the finding of the *Treponema pallidum* in the brain of paretics and the spinal cord of tabetics, we have come to consider all forms of syphilitic nervous disease including the so-called parasymphilitic nervous diseases primarily as inflammatory or degenerative reactions to the invasion of the *Treponema pallidum*, and to regard the various clinical manifestations as explainable by a consideration of whether this organism has invaded and caused changes in the brain, spinal cord, their coverings, the cranial or spinal nerves, or the blood vessels which supply these parts.

#### CLASSIFICATION OF SYPHILITIC NERVOUS DISEASE

The disease may be classified according to the site of involvement, i. e., the brain, cord, spinal or cranial nerves, sympathetic system, or according to whether the lesion involves the meninges, the parenchyma, or the vessels, or all of these structures in one or more parts of the nervous system. It has seemed to us to be necessary to differentiate between the forms of syphilis of the nervous system showing involvement of the membranes and of the vessels, the "syphilis meningovascularis" of Head and Fearnside,<sup>1</sup> and the parenchymatous forms, the syphilis centralis of Head and Fearnside, especially in view of the difference in response to therapy.

#### CLASSIFICATION OF HEAD AND FEARNSIDES

##### *I. Syphilis Meningovascularis*

Cerebral forms.	Muscular atrophy.
Hemiplegia.	Lateral and combined degenerations.
Affections of the cranial nerves.	Epilepsy.

##### *II. Syphilis Centralis*

Dementia paralytica.	Optic atrophy.
Tabes dorsalis.	Gastric crises.
Muscular atrophy.	Epileptic manifestations.

To show the complexity of the matter of classification of syphilitic nervous diseases according to any scheme, a collection of the various forms and combinations of forms of these diseases according to the anatomic lesion found, as published by Southard and Solomon,<sup>2</sup> is presented:

*Meningeal Neurosyphilis*

Gumma of dura mater.	Syphilitic root neuritis.
Gummatous meningitis.	Syphilitic transversemyelitis.
Syphilitic meningitis.	Syphilitic neuritis.
Syphilitic cranial nerve palsies.	Syphilitic epilepsy.
Syphilitic bulbar palsy.	Syphilitic muscular atrophy.

*Vascular Neurosyphilis*

Syphilitic arteriosclerosis.	Syphilitic apoplexy.
Syphilitic cerebral thrombosis.	Aneurysm.
Syphilitic epilepsy.	

*Parenchymatous Neurosyphilis*

Gumma.	Syphilitic epilepsy.
Cerebrospinal sclerosis.	Tabetic psychosis.
Syphilitic paranoia.	Syphilitic muscular atrophy.
Syphilitic chorea.	Syphilitic neuritis.

*Meningovascular Neurosyphilis*

Cerebral syphilis.	Cerebrospinal syphilis.
Syphilitic epilepsy.	

*Meningoparenchymatous Neurosyphilis*

Cerebral syphilis.	Tabes dorsalis.
Cerebrospinal syphilis.	Erb's syphilitic spastic spinal palsy.

*Vasculoparenchymatous Neurosyphilis*

Cerebral syphilis.	Paretic neurosyphilis.
Cerebrospinal syphilis.	Lissauer's general paresis.

*Meningovasculoparenchymatous Neurosyphilis*

Cerebral syphilis.	Paretic neurosyphilis.
Cerebrospinal syphilis.	Taboparesis.

*Doubtful (Toxic? Irritative?) Neurosyphilis (?)*

"Paresis sine paresi."	Syphilitic paranoia.
Syphilitic neurasthenia.	Syphilitic polyuria, polydipsia.
Tabetic psychosis.	Syphilitic neuralgia.

CEREBROSPINAL SYPHILIS

In *cerebrospinal* syphilis the lesion may take the form of a single gumma or of multiple gummata, and as a rule these lesions are

not amenable to cure by antisyphilitic treatment. If localizable, gummata should be treated surgically like any other neoplasm of the brain or cord, after a fair trial has been accorded intensive medicinal treatment. A diffuse gummatous infiltration in the membranes of the brain or cord, which is usually associated with some change in the underlying tissue, lends itself to improvement if not cure by means of the treatment to be advocated, if it is not too long delayed. A meningeal inflammation can be cured, as in Cases 1 and 2, but if the subjacent tissue has been markedly involved, it may be irreparably injured and naturally can not be restored to function, as in Case 3. This is especially true when there is destruction of tissue due to occlusion of terminal blood vessels. The resulting myelitis and encephalitis are usually accompanied by permanent destruction of function, dependent in its severity on the extent of the lesion and the physiologic activity of the part involved. The meningomyelitis and meningoencephalitis of Alzheimer<sup>3</sup> and others constitute a group of cases which come under this category. Some of the epileptic conditions due to more or less superficial involvement are sometimes curable.\* In the spinal cord the meningomyelitic process is one which, if treated early and energetically, admits of complete or almost complete restitution of function. If, however, the inflammatory process is accompanied by degenerative lesions in the cord tracts, or even, as occasionally occurs, in the anterior horn cells, as in Case 4, the antiluetic treatment can only bring about improvement in the condition, but can not fully restore the function in the degenerated tissues. Sometimes the parenchymatous degeneration which accompanies the acute stage of meningomyelitis or encephalitis advances rapidly beyond the possibility of a cure by any means at our command, as in Cases 3 and 5. Syphilitic disease of the blood vessels (due to the invasion of the lymphatics of the vasa vasorum in the adventitia of the vessels) offers an opportunity for the action of drugs introduced into the circulation. This is true of the small vessels of the brain and cord, although when the lesion involves large vessels, complete

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\*Syphilitic epilepsy, as a glance at the charts will show, is not a clinical entity. The condition may be focal due to gumma or local meningitis or the result of an old or early vascular lesion or general. These symptomatic epilepsies in the course of a neurosyphilis are to be differentiated from epilepsy due to meningitis or diffuse meningoencephalitis. Epileptic seizures are not uncommon in general paresis. The so-called parasymphilitic epilepsy of Fournier is similar in most respects to idiopathic epilepsy. The condition is associated with positive blood and spinal fluid reactions, but in many of these cases no gross pathologic changes are found at autopsy. These cases rarely respond to treatment.

restitution may be impossible. The pathologic process in the blood vessels of the brain often causes occlusion early before our syphilitic remedies have an opportunity of acting effectively. The result is a destruction of that portion of the brain supplied by the vessel involved. As the vessels are usually terminal, the loss of function is dependent upon the size of the vessel and the region supplied by it. Restitution is sometimes considerable, as in Case 6, but only too often restoration of function is impossible, as in Case 7. The possibility of the syphilitic lesion being confined to the blood vessels almost entirely must be borne in mind, especially in view of the possibility of sudden extensive nervous involvement, frequently in young subjects.

#### TABES DORSALIS

We regard the pathologic process which is present in *tabes dorsalis* as a primary neuronal degeneration; and the occasional meningeal involvement which is a factor in the early cases, as well as the perivascular lymphocytosis, the presence of plasma cells and the growth of glia are all to be regarded as reactions to the presence of spirochete. Indeed Knowles and Mott<sup>4</sup> and Warthin<sup>9</sup> demonstrated the presence of *Spirochete pallida* in perivascular cell infiltrates in a recently reported case. It has been asserted by certain investigators, especially Nageotte,<sup>5</sup> that the meningeal irritation surrounding the posterior ganglia and nerve roots in tabes is the primary condition responsible for the neuronie degeneration, which is secondary. We can not accept this view and hold with Ferrier<sup>6</sup> that "the intramedullary degeneration of tabes is often well marked when the posterior roots exhibit no appreciable change and no indication of a local neuritis." Ferrier maintains that there is no posterior meningitis of a syphilitic nature, that the results of anti-syphilitic treatment speak against this possibility, and that the presence of a lymphocytosis in the spinal fluid can not be advanced as a conclusive argument. True tabes must be differentiated from pseudotabes due to a syphilitic involvement of the meninges of the cord in which there is incidentally involvement of the posterior roots and secondary degeneration of the posterior columns. This condition was first pointed out in 1888 by Oppenheim<sup>7</sup> and by Eisenlohr<sup>8</sup> as a condition which was susceptible to improvement or even cure by the antisiphilitic remedies then in vogue. These cases,

it must be stated, closely resemble true tabes in many respects except in their course. They rarely have a true Argyll Robertson pupil, although a certain amount of amblyopia may occur. No doubt the reported instances of cure of tabes, with a return of knee kicks, the eradication of bladder symptoms, and the return of sexual power after one or another form of treatment are cases of this kind.

#### OPTIC ATROPHY

From a pathologic standpoint optic atrophy is analogous to tabes in that there is a primary ascending degenerative lesion of the nerve fibers beginning in the ganglion cells of the retina. The optic neuritis occurring in cerebrospinal lues is secondary and descending and is due to an inflammatory process about the nerve trunk or in the region of the chiasm (basal meningitis, gummatous infiltration). Thus syphilitic optic nerve lesions are primary or parenchymatous as in the tabetic form and secondary or interstitial as in optic neuritis occurring in cerebrospinal lues which later may eventually go on to secondary optic atrophy. Both types are due to spirochetal invasion. The primary form may be accompanied by a certain amount of active inflammation just as in true tabes there may be a certain amount of meningeal inflammation in the cord. The recent studies of Stargardt,<sup>9</sup> unconfirmed as yet, attempt to show that the tabetic optic atrophy begins in the course of the optic nerve and not in the retina, as has been generally accepted. The lesion is usually an exudative one in the intracranial portion of the nerve, the degeneration of the retina being secondary, and hence similar to the interstitial lesion of cerebrospinal lues. The fact that the usual forms of treatment have been so uniformly unsuccessful in bringing about a cure in optic atrophy, whereas other interstitial lesions of a syphilitic nature are more or less readily amenable to treatment, tends to throw a doubt on the correctness of this view.

#### DEMENTIA PARALYTICA

In *dementia paralytica* we are dealing with an invasion of the brain by the *Treponema pallidum* causing a parenchymatous degeneration and a more or less active mesoblastic response. The spinal cord may simultaneously present lesions of the tabetic type.

The studies of Warthin are worthy of serious consideration. Ac-

According to this investigator the characteristic and substantiative pathologic evidence of true paresis is the widespread periarterial infiltration of lymphocytes and plasma cells with eventually parenchymatous destruction. Similar lesions in the intracranial vessels to those in the intracortical ones were found, and these were in all respects similar to those of syphilitic aortitis. According to Orton's view the onset of the psychosis means the beginning of degeneration in the parenchyma from the foci of infection in the vascular structures. It may therefore be that intensive treatment might prevent the development of the parenchymatous degeneration if begun while the lesion is still interstitial in type.

Warthin found focal infiltrations of lymphocytes and plasma cells in both the brain and cord in cases not clinically tabes or paresis. These infiltrations were perivascular and were occasionally accompanied by proliferative vessel changes. They differed only in number and degree from foci found in paresis and tabes. In one case of secondary lues dying from salvarsan poisoning Warthin found such foci. These findings led him to speculate as to whether every case of syphilis is not to a slight degree a case of paresis or tabes and in keeping with the finding occasionally of the so-called borderland cases pathologically. As Warthin states "such infiltrations represent simply the local reaction to the presence of spirochetes; and their relation to paresis and tabes may be simply one of degree, with reference to the number of infecting organisms, the degree of intoxication produced, and the resulting destruction of nerve tissue and functional disturbance produced."

We have no therapeutic agent at our command today which can completely counteract the action of the spirochete in causing neuronal degeneration once they have reached certain nonvascular parts of the brain and cord.

Our drugs have effect insofar as they destroy those spirochetes which can be reached by the medicaments and which have not become resistant to their action. Unfortunately, in fully developed dementia paralytica, the masses of spirochetes for the most part are situated in foci away from the blood vessels and difficult of approach by drugs which are administered through the circulation. Attempts to reach them through the spinal fluid we be-

lieve also to be futile, not only because the spinal fluid is not the proper method of physiologic approach to the parenchyma of the brain or cord, as we shall show, but because practically the introduction of the drugs and sera now at our command into the spinal fluid has not resulted in any lasting curative results. This renders the hope of a complete cure of the pathologic process at present slight. Remissions in paresis are spontaneous or induced by therapy and may possibly be regarded, as Ehrlich<sup>10</sup> has pointed out hypothetically, as intervals caused by "antibody formation." The duration of the intermission is dependent upon the extent of the spirochetal mass bound by the "antibody formation." The disease process flares up again when the organisms resume their activity. Spirillolysis occurs in the free interval, the breaking down of the organisms causing endotoxin liberation. Occasionally when treatment is very intensive, this endotoxin liberation may overwhelm the patient rapidly during or soon after the cessation of treatment, as in Case 8.

However, if as is possible, the organisms of the disease thus early are already firmly intrenched in the parenchyma of the brain, though possibly latent in their pathogenicity, we fear that with the present therapeutic means at our command we can not effect a cure. Unfortunately, very early biological changes in the spinal fluid are due to superficial meningeal inflammation, while in the primary neuronie decay, such as exists in tabes and paresis, as we have pointed out, the meninges may not show any irritative reaction and the fluid may be entirely normal at this stage, although the neuronal degeneration may be progressive. This brings up the interesting question concerning the neuropathic tendency of certain strains of the *Treponema pallidum*. Do only certain strains of this organism possess the power of early invasion of the central nervous system, or have all strains of the organism this selective power provided certain necessary predisposing factors are present?\*

\*Nichols and Hough<sup>11</sup> succeeded in isolating a strain of *Treponema pallidum* from a neuro-  
recidive which invaded the cornea of rabbits repeatedly and constantly even before the appearance of a lesion in the testicle in which the fluid was injected. The patient died of a meningoencephalitis within a few months after infection. The strain isolated by culture persisted in causing a keratitis and chorioretinitis in rabbits, causing Nichols to conclude that the nervous lesion was explainable by the character of the strain. In studying the cultural characteristics of ten strains of *Treponema pallidum* Noguchi<sup>12</sup> noted that organisms of a certain type constantly produced lesions of a certain character in rabbits. Under artificial conditions these organisms kept their characteristics for over a year. Two strains of pallida from parietic brains were found to be of lower virulence requiring up to one hundred and two days before lesions were produced in rabbits' testicles, the usual skin strains causing lesions in twenty-eight days.



It would seem that, given an infection with a highly neurotoxic strain in a more or less susceptible individual, lesions in the nervous system should occur within a reasonably short time after the primary infection, say within the first year or two, as occasionally does happen in cerebrospinal syphilis. If the individual possesses a high degree of nervous immunity, the organisms that wander into the nervous tissue are at once destroyed or rendered innocuous. They may become more or less encapsulated in the cerebrospinal system without much local damage and with perhaps certain changes of a biological nature in the spinal fluid if the meninges are involved. After a number of years these inert groups of organisms may assume a pathogenic character and, for one reason or another, perhaps because they have been altered by their long residence in the human host, set up lesions of a peculiar pathologic nature which heretofore have been known as parasymphilitic lesions. Why these organisms should become active again years after infection is as yet unknown to us. That they can exist in a viable state in small groups, often contiguous to the blood vessels, for years after the initial infection without much microscopic change in the surrounding tissue, has been proved conclusively by the work of Warthin.<sup>13\*</sup> That those individuals who later become victims of paresis and tabes possess some degree of natural immunity is evidenced by the fact that in many of these syphilitics the early manifestations of the disease were slight or entirely overlooked in spite of inadequate treatment or even in the entire absence of antisymphilitic treatment after acquisition of the disease.

Further, the long period of time elapsing between the infection and the occurrence of lesions in the central nervous system, and the more or less chronic course of many of the forms of syphilitic nervous disease bespeak a certain degree of general and local resistance. The individual may possess, when infected, only a fair

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\*Graves<sup>14</sup> found that the blood of a paretic kept sealed in an ampule at body temperature for a few days could successfully be introduced into the testicle of rabbits with the production of typical local and generalized lesions within four weeks. While most of his experiments were negative, he was able to isolate a strain of *Treponema pallidum* that produced a typical keratitis in rabbits. Graves could not demonstrate the organism in the blood of this paretic, nor could he cultivate the germ from it, although from it he was able even after weeks or months to produce typical lesions in rabbits. This led him to think of the possibility of a latent or resting stage in the organism's cycle little known as yet and also the possibility of a very resistant form of the organism capable of lying dormant for years until favorable growth conditions obtained. These conditions may arise after years of latency in syphilis with the production of neurosyphilis.

degree of resistance to the organism, though for some reason or other, very possibly because of inadequate treatment, certain groups of organisms are not killed and remain alive though dormant in some of the remote viscera of the body. From time to time these viable spirochetes wander into the blood stream. If through mental or nervous strain or stress a locus resistantiae minoris is found in the nervous system, infection occurs, depending in its severity and extent on the virulence of the infecting organism and the degree of resistance offered by the invaded tissue.

Infection occurs then either by the lighting up of dormant groups of spirochete in the nervous tissue or by an invasion of the nervous system by way of the blood stream from some remote latent or active focus. In any event, the nervous tissue is involved primarily and the spinal fluid secondarily.\* Biological changes in the fluid, the erroneously so-called infection of the spinal fluid, is secondary and merely an evidence of reaction or inflammation in or contiguous to the membranes. Infection of the nervous system, however, does not occur via the fluid, a fact to be borne in mind in discussing the rationale and limitations of intrathecal treatment.

From what has been said it is evident that there are frequently two distinct types of reaction to the invasion of the spirochete. The one is similar in its pathology to active syphilitic involvement, interstitial in type, involving principally the membranes, occurring rather early in syphilis, and only to a secondary degree

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\*A search of the literature reveals comparatively few instances of the finding of spirochetes in the spinal fluid, and Zinsser, Hopkins, and Gilbert<sup>15</sup> doubt the existence of ultra-microscopic forms.

Uhlenhuth and Mulzer,<sup>16</sup> in 1913, reported negative findings from the inoculation of rabbits with the spinal fluid of seven recently syphilitic individuals and four tabetics and general paresis, although later they were able successfully to inoculate a rabbit's testicle with the spinal fluid of a cerebrospinal luetic. No spirochetes could be found by searching the fluid and there was only a moderate pleocytosis in it. Hoffman<sup>17</sup> successfully inoculated an ape with the spinal fluid of an early luetic with a papular syphilide. Nichols and Hough<sup>18</sup> also inoculated a rabbit's testicle successfully with the fluid of an early cerebrospinal luetic. Steiner<sup>19</sup> got three positive results in twenty cases of early lues without any abnormality being present in the fluid. All his nineteen cases of tabes, paresis, and cerebrospinal lues were negative.

Fruhwald and Zaloziński<sup>20</sup> in twenty-three experiments got positive results in one case of primary lues with a rash and in one case of late secondary lues and in a case of early syphilitic meningitis and a case of tabes. Reasoner<sup>21</sup> was successful in inoculating and cultivating the spirochete in one case of cerebral lues and it was this strain that showed peculiar characteristics suggestive of a neurotropic tendency. Sezari and Paillard<sup>22</sup> found the organisms in the dark-field microscope in a case of hemiplegia, and Gaucher and Merle<sup>23</sup> found them similarly in the ventricular fluid in a hemiplegic. Levaditi, Marie and Bankowski<sup>24</sup> found them in the ventricular fluid of a paretic. On the whole, search of the fluid in all types of cases has been rarely successful. In eight cases of neurosyphilis Wile<sup>25</sup> was unable to inoculate a rabbit's testicle successfully, although it was possible to find the organisms in the rabbit's testicle a few days after inoculation in most of the cases. He believes the spinal fluid is infectious at times even though the organisms can not readily be found.

the brain or cord substance proper, with or without marked changes in the blood vessels, and with occasionally a certain amount of tissue destruction due to vessel closure. The other type is usually more chronic and the lesions occur later, being chiefly of a parenchymatous nature with neuronie degeneration primary and irreparable. The first type is what is commonly known as cerebral or cerebrospinal lues; the second, the so-called parasyphilitic conditions—as tabes and paresis. It is essential to bear these broad conceptions of the pathologic lesions in mind, since it will be seen that whereas changes of the interstitial type are more or less susceptible to retrogressive change by treatment, those of the primary degenerative or parenchymatous type are usually progressive, occasionally becoming stationary for a certain period of time spontaneously or as a result of treatment.

In the present stage of our knowledge a definite differential diagnosis between cerebrospinal lues and early dementia paralytica\* is often impossible even with the aid of all the known serologic reactions at our disposal. Indeed it is difficult occasionally for the trained neuropathologist to decide definitely by means of careful histologic examination unless it be possible to obtain the brain within an hour or two after death and by means of the ultramicroscope, tissue examination, or rabbit inoculations, obtain evidence of the presence of spirochete in the parenchyma or other characteristic features of the disease. Clinically the diagnosis must often await the test of time as in Cases 9, 10, 11 and 12.

#### CEREBROSPINAL FLUID REACTIONS

The scientific treatment of syphilis of the nervous system is in a great measure dependent upon the facts ascertainable by an analysis of the spinal fluid. The direct etiologic relationship between the *Spirochete pallidum* and all forms of syphilitic nervous disease having already been pointed out, and in view of the

\*The question of diagnosis in the preparetic stage brings up the important point as to the permissibility and advisability of brain puncture as originated by Neisser<sup>26</sup> and practiced by Foerster.<sup>27</sup> In a series of sixty-one punctures active spirochete were found under the dark-field microscope in twenty-seven cases (44 per cent). If it were possible in cases of persistent blood Wassermann reactions with positive spinal fluid serological tests including a positive gold sol paretic curve to determine in the brain the presence of histologic changes or of the *Spirochete pallida*, the procedure might be justified as a means to prevent possibly the certain ravages of the further course of the disease. Another procedure that has had little attention paid to it is the differential cytologic count of the spinal fluid—as pointed out by Orton.<sup>28</sup> The presence in the fluid of a preponderating number of plasma cells may also prove of significance.

fact that a pathologic spinal fluid, as a result of syphilitic infection, may long antedate the appearance of definite clinical signs of involvement of the nervous system, it is evident that examination of the spinal fluid is of great importance not only in diagnosis but also in planning treatment. In constitutional syphilis the occurrence of an abnormal fluid should draw attention to the possibility of beginning changes in the neuraxis and lead to the institution of appropriate treatment designed to check the progress of or eradicate entirely the infection. In cases where an involvement of the neuraxis has been definitely established by the occurrence of subjective and objective symptoms, the data revealed by an analysis of the spinal fluid are of value in diagnosis, in prognosis, and also, as will be shown, in planning and carrying out treatment.

In order to indicate to what extent one can rely upon the biological reactions of the blood and spinal fluid alone in diagnosis and in prognosis, it is necessary to describe the incidence of these reactions in the various types of syphilitic nervous disease under discussion; to show that while the tests are positive in a high percentage of certain types of the disease, they are frequently lacking entirely in others, and to emphasize the fact that when present they are sometimes subject to spontaneous fluctuations and even to more or less rapid disappearance without treatment. It is our opinion that it is unwise frequently to rely solely upon laboratory data as diagnostic and prognostic criteria, but that equal weight should be placed upon the facts revealed by a clinical study of the case and of a knowledge of the pathologic process responsible for the condition.

In the late primary or early secondary stage of syphilis, coincident with the dissemination of the spirochete throughout the body, the Wassermann reaction in the blood becomes positive. At this time examination of the spinal fluid in a high percentage of cases studied shows changes in the cell count and globulin reaction indicative of irritation of the meninges. Ravaut,<sup>29</sup> Altman and Dreyfus<sup>30</sup> found in from 70 to 80 per cent of secondary cases an increased globulin reaction or an increase in the cytologic count above the normal of five to seven cells to the cubic millimeter. In a small percentage of cases in this period a

positive Wassermann reaction in the spinal fluid has been found, and in these patients there were already definite clinical signs of changes in the nervous system. The Wassermann reaction occurring at this time is unquestionably, we believe, positive proof of involvement of the nervous system by the syphilitic infection. It is a question in our minds, however, whether the presence of the positive globulin reaction and increased cell count at this time, in the absence of definite objective or subjective nervous symptoms, constitutes *eo ipso* absolute evidence of nervous tissue change other perhaps than a superficial and evanescent meningeal irritation. It is certain that in the majority of these early cases showing spinal fluid changes (pleocytosis, globulin increase) the reaction in the fluid subsequently becomes normal either spontaneously or after treatment. In Dreyfus's series the reactions persisted in about 12 per cent of the patients, which corresponds closely to the number of syphilitics who subsequently develop definite involvement of the neuraxis. In our opinion the presence of increased pressure in the spinal fluid is of doubtful diagnostic significance owing to the great difficulty of accurately measuring the fluid tension and on account of extreme variations due to extraneous factors, such as the position of the patient, the depth of inspiratory efforts, the size of the needle used for puncture, and its position in the subarachnoid space.

Thus while it is apparent that in early syphilis, active or latent, the only evidence of the presence of spirochete or their toxins in the nervous system may be found in the biological response in the fluid, it is still a mooted question whether the pleocytosis and globulin increase are transient or the forerunner of one of the forms of syphilis of the nervous system to which we have already referred. In a number of cases under observation a persistent positive blood Wassermann has led to the discovery of a positive Wassermann in the spinal fluid, increased cells, and globulin, without objective or subjective symptoms of neurosyphilitic involvement, as in Cases 9 and 28. These facts doubtless point out the necessity for continued observation and biological examination of patients presenting such changes, and for the prolongation of the period of treatment until they are eradicated. This is especially desirable in patients in whom the Wassermann reaction in the blood per-

sists for a considerable period of time after the cessation of treatment and in latent or tertiary cases in which treatment has been neglected. In all these cases lumbar puncture should be done.

The initial and early secondary periods having elapsed, the patient enters the late secondary and early latent periods, and from this time throughout the later years following the luetic infection the occurrence of a pathologic spinal fluid is of great significance and always indicative of nervous tissue change. The biological response is in the nature of a positive Wassermann reaction (quantities of fluid used in the test 0.1 c.c.-1.0 c.c.), increase in the number of cells (usually lymphocytes) (five to seven cells to the cubic centimeter—normal), and an increase in the globulin reaction of the fluid (as ascertained by the Noguchi butyric acid or other test).

In lesions of the nervous system of the interstitial type (meningovascular), *cerebrospinal lues*, the Wassermann test of the spinal fluid is positive in from 20 to 80 per cent, depending upon the type and chronicity of the lesion, and the amount of treatment received. In the pure cerebral types (Head<sup>32</sup>) all the reactions including the Wassermann may be negative in nearly all the cases. In the endarteritic types of cerebral spinal lues likewise all the reactions are frequently negative. In the meningomyelitic and meningoencephalitic types, on the other hand, the reactions are all usually positive. The Wassermann reaction is present in the smallest quantities used, the cells are increased, frequently over a hundred to the cubic centimeter, occasionally a thousand or more, and the globulin is markedly increased (one to two plus). In these cases the pleocytosis and globulin reaction are in direct proportion to the severity of the meningeal inflammation.

In *tabes dorsalis* the spinal fluid is positive at some stage of the disease, but especially early in the disease. The Wassermann reaction is positive in from 70 to 80 per cent of all cases, the globulin reaction is usually positive, and the cells are moderately increased, rarely being more than a hundred or two to the cubic millimeter. High cell counts, indicative of a marked meningeal inflammation, are uncommon in true tabes, and should arouse a suspicion of pseudo-tabes, or of beginning paresis, as in Case 11. In the late degenerative types of the disease all the reactions may be negative.

In Erb's<sup>33</sup> *spastic paraplegia* the reactions are apt to be positive early in the course of the disease, but it is our experience that there is a decided tendency towards a rapid subsidence of all the reactions, even without much treatment, as in Cases 29 and 30.

The biological reactions in *general paresis* are almost always positive both in the spinal fluid and in the blood. The Wassermann reaction in the fluid is positive in the lowest quantities used in the test (0.1 c.c.), the cells are increased to a moderate degree, usually not over a hundred to the cubic millimeter, and the globulin is also increased. The colloidal gold solution reaction gives the so-called paretic curve, which is regarded as characteristic of general paresis, but which is also occasionally given by other specific nervous conditions, as in tabetics and cerebrospinal luetics without any signs of intellectual deterioration. So constant are the above biological phenomena in this disease that in their absence the diagnosis should be looked upon as unproved unless the subjective and objective symptoms are absolutely conclusive. The few exceptions are found in late degenerative stages of paresis and tabo-paresis and in the occasional juvenile types, the result of hereditary syphilis.

#### CLINICAL VALUE OF BIOLOGICAL REACTIONS

Having considered the occurrence of the various biological reactions in the types of syphilitic nervous disease commonly met in practice, a discussion of the value of these reactions in determining the course and prognosis of the disease is essential. We must accept as a fact the statement that a positive Wassermann reaction in the blood means the presence of active or latent constitutional syphilis and that a positive Wassermann reaction in the spinal fluid is likewise evidence of an involvement of the nervous system by the syphilitic "virus." A negative reaction in the fluid, however, is not conclusive proof of the absence of nervous involvement nor is a change of the reaction from a positive to a negative one absolute proof of the subsidence or cure of a once existent lesion. In support of the former statement we need only point out the numerous cases of endarteritis of the brain and cord vessels due to syphilis in which frequently, as we stated,

the reactions (Wassermann, cytology, and globulin) are all negative in the fluid (and occasionally the Wassermann reaction in the blood also) and mention the cases of spastic paraplegia and even occasionally tabes and dementia paralytica with negative reactions. Nervous involvement due to congenital syphilis also frequently gives a negative reaction, especially if the nervous involvement occurs late, say after puberty. The occurrence of syphilis of the nervous system of the vessel type in comparatively young individuals often without marked premonitory symptoms of nervous involvement and with entirely negative biological reactions in the fluid points out the great care necessary in using a negative fluid as a sign of good omen in prognosis as in Cases 6, 29, 31 and 32. Lesions of this type cause marked destruction of nervous tissue and correspondingly great disturbance of function from which recovery is only too often impossible. Such cases may give a positive blood reaction, and in the event of a persistent blood reaction in a young or middle aged individual, with or without some signs referable to the nervous system, as for example, sluggish pupillary reactions, persistent headaches, optic neuritis, together with evidence of general vascular or renal involvement, the possibility of cerebral vessel change must be borne in mind and proper treatment instituted. Although all the reactions in a case of spastic paraplegia may be negative in the fluid, yet the pathologic process may be progressive, as in Cases 7 and 30. We have seen a number of cases with marked symptoms referable to the nervous system, in some of which there was a previous history of syphilis but in which all the reactions, both in the blood and in the fluid, were negative, markedly improved by antisypilitic treatment as in Cases 33, 34 and 35. In some isolated instances all the reactions may be negative with the exception of the cytology which may show an increase above the normal as in Cases 2 and 36. In a few cases a cell count of five hundred or more lymphocytes to the cubic millimeter was found and improvement following intravenous therapy was marked, as in Cases 1 and 11. Cases of tabes dorsalis and especially tabetic optic atrophy not infrequently give entirely negative biological reactions in the fluid and in the blood, with occasionally a slight increase in the cells or in the globulin reaction, yet the symptoms of the disease may be marked and the course of the



disease progressive, as in Cases 29 and 37. Therefore, the statement of Fordyce<sup>34</sup> that with all the biological reactions negative in the spinal fluid there is assurance against a relapse in the disease, must be accepted with great reservation. In certain types of cerebrospinal lues, especially of the interstitial or exudative type with superficial meningeal involvement, a progressive change in the fluid from positive to negative is a sign of good prognostic significance if taken together with progressive clinical improvement of the patient, as in Case 23. On the other hand, in cases of this kind where the biological reactions persist in spite of treatment, even though clinically there is marked improvement, especially in the subjective symptoms, the prognosis should be guarded and continued treatment advised, as in Case 39.

Instances are not lacking in which the nervous disease has been apparently checked for a great many years in the presence of positive biological reactions, as in Case 38, so that one can not be dogmatic in stating that the persistence of positive biological tests in the blood and fluid are always of bad prognosis, but it has been our practice to advise periodic treatment in these cases, even though the patients often felt that it was superfluous. We have treated some patients for a number of years intravenously without affecting the Wassermann test in the fluid. The cytology is usually gradually diminished to within normal limits and occasionally the globulin also is reduced to normal. Finally, after a number of withdrawals of spinal fluid the Wassermann reaction, after persisting for a long time as stated, may within a few weeks or months become entirely negative and may remain negative for months, gradually relapsing or may remain negative permanently, as in Cases 20 and 40.

We occasionally see patients with nervous disease (usually cerebrospinal lues, occasionally tabes) in whom the blood reaction is persistently negative, even after provocative injections of salvarsan or mercury, with positive biological reactions in the fluid. In cases of this type, especially, intraspinal therapy has been recommended as of greater value than intravenous treatment. However, examination of these patients usually reveals that the lesion is not confined to the nervous tissue alone, but that there is coincidentally change in the vessels or large viscera, without the reaction in the blood. Such cases should therefore be treated intravenously even

though an effort be made by intraspinal treatment to reach a localized focus in the spinal cord.

In cases of cerebrospinal syphilis the presence of an isolated symptom often brings up the question as to whether this is a sign of active disease or a residuum of a once existent infection. The stiff and irregular pupil, the absent or diminished knee jerk or Achilles jerk, or a diplopia are examples. In these cases negative biological reactions and the absence of subjective symptoms are presumptive but not absolute evidence of a quiescent or cured process, while the presence of positive reactions in the fluid is contributory evidence of an active though possibly localized lesion. As regards the effect of treatment in general on the various biological reactions, it may be stated briefly that the cell count in the fluid is usually rapidly influenced by any form of persistent treatment. After one or two intravenous treatments a high cell count from an exudative meningeal process in cerebrospinal lues or pseudotabes may drop almost if not quite to normal. Occasionally frequent lumbar puncture has the same effect. The cytologic count is subject to marked spontaneous fluctuations, as Newcomb, Mitchell and Darling<sup>35</sup> have also shown, and even during treatment wide fluctuations may occur. The globulin reaction is less susceptible to change, although on the whole it follows the cell count fairly closely in its variations. The Wassermann test in the fluid is most constant in its presence and less easily influenced by treatment of any kind than either of the above reactions. In cerebrospinal lues it is most easily affected, and in certain types disappears spontaneously or after treatment with the cessation of the exudative meningitic lesion. In tabes it may be most persistent during the activity of the disease, despite intensive treatment, and may persist up to the very end, or with the onset of marked degenerative lesions the reaction may become negative. Spontaneous fluctuations in the strength of the spinal fluid Wassermann within amounts varying from 0.1 c.e. to 1.0 c.e. occasionally occur but are uncommon. The persistence of a positive Wassermann in the fluid in tabes may be interpreted with the presence of a paretic curve (gold solution) in the fluid as a possible sign of the eventual development of paresis, but we are not inclined to subscribe to this view at present.

In general paresis treatment may cause diminution in the cell count or globulin reaction, but the Wassermann test is rarely influenced. It rarely even fluctuates but is usually positive in all dilutions, and the paretic curve persists despite treatment. In late degenerative types of the disease the fluid may gradually become normal; or if treatment is being administered it may be attributed to this fact. This fallacy must be borne in mind in estimating the value of any forms of treatment in this as well as other types of syphilitic nervous involvement.

#### TREATMENT

Treatment of syphilitic disease of the nervous system should aim at as complete an eradication of the active syphilitic process as is compatible with the well-being of the patient. Where, on account of the nature of the pathologic process, symptoms of the disease persist in spite of our best efforts to remove the infection, we should endeavor to retard its progress and relieve the symptoms so far as possible.

Certain broad classifications can be made on clinical grounds relative to the degree of improvement which may be expected and the form of therapy best suited to bring about either cure or improvement.

*Group I.*—This group includes cases of early cerebrospinal syphilis (meningitis, meningomyelitis, meningoencephalitis, cerebral endarteritis, syphilitic epilepsy, optic neuritis, pseudotabes due to radiculitis and meningitis, ophthalmoplegia), early tabes dorsalis, early cases of Erb's spastic paraplegia, and those early cases of syphilis without nervous symptoms at all or with very persistent cephalalgia presenting biological changes in the spinal fluid. In all these types where the lesion is interstitial (as pointed out in discussing the pathology of nervous syphilis) intensive treatment is often successful in effecting a complete clinical cure. In the vascular lesions the prognosis must be more guarded as to cure or even marked improvement. In early tabes, the subjective symptoms may be cured and the disease arrested apparently for years, but it should be kept in mind that true tabes, with its primary neuronie decay is apt to be slowly progressive over a period of many years with intervals of active and quiescent symptoms, even

if intensive treatment is begun early. Prognosis should, therefore, be very guarded as to complete cure even with a coincidental improvement or disappearance of the biological reaction in the spinal fluid.

If the symptoms are very urgent and life is in danger, the most intensive intravenous therapy is indicated. Salvarsan or one of its safe substitutes (arsenobenzol, arsphenamine, novarsenobenzol-Billon) should be given intravenously every day or every other day in doses of 0.2 gram to 0.3 gram, until a total of 1.0 to 1.2 gram is given in every period of seven days. This very intensive therapy can be safely kept up for a period of from four to eight weeks. It is not usually necessary to give the drug more than three times a week for more than four to six weeks. On the alternate days injections (deep intramuscular) of mercury bichloride may be given in doses of from one-fifth grain every other or third day or mercury salicylate one to two grains every fourth or fifth day. Where the lesion is of the gummatous type the iodides should be administered in addition to the salvarsan treatment in doses up to 30 to 60 grains three times a day. Where the symptoms are not so urgent, as in the more chronic cases of cerebrospinal lues and tabes, we usually give from 0.8 gram to 1.0 gram of salvarsan each week with or without injections or inunctions of mercury. The inunctions are often better borne by individuals with ataxia of the lower extremities. In these less urgent cases the intravenous injections are kept up for about six to eight weeks. At the end of this time the patients are given a rest of from one to two months to aid in elimination of the arsenic and mercury.

In cases belonging to this group where the irritative symptoms due to meningeal involvement are pronounced, and where the biological reactions are also marked in the spinal fluid (marked increase in cells and globulin; positive Wassermann reaction in 0.1 to 1.0 c.c.), or where these reactions persist in spite of repeated intravenous treatments, lumbar puncture every week or fortnight with a withdrawal of 20 to 60 c.c. of fluid with or without the replacement of the fluid in part by nonmedicated patients' serum, normal serum, or normal saline is indicated. The tappings are not persisted in unless relief is afforded. Intraspinal treatment is of course contraindicated in the bulbar types of involvement.

*Group II.*—In this group we place the more chronic cases, espe-

cially the more persistent types of cerebrospinal lues and tabes with persistent positive reactions in the blood and spinal fluid and mild subjective symptoms.

These patients should receive salvarsan twice a week where feasible or every fifth or sixth day in somewhat larger dosage than in Group I (0.3 to 0.4 grams) for a period of six or eight weeks, followed by injections of mercury salicylate (1 to 2 grains) every fifth day for a period of two months, or by a course of mercurial inunctions. Where injections or inunctions are not feasible, the protiodide of mercury may be prescribed in from one-eighth to one-quarter grain three times a day for a few weeks, alternating with iodide therapy for a similar period of time, watching carefully for evidence of mercurialization.

In Group I after the urgent symptoms are abolished, it is not necessary to maintain the very intensive salvarsan therapy for the full period of eight weeks, but the patients may at the end of a month be treated like the cases of Group II if improvement has been satisfactory, the drug being given not oftener than twice a week or thrice in a fortnight.

In both of the groups of cases when treatment is resumed after the completion of the rest period the urgency and nature of the symptoms remaining determine the plan of procedure to be adopted. Where symptoms like pains, paresthesias, crises, and bladder and rectal disturbances persist, a second course of salvarsan intravenously followed by mercury is advisable, but the salvarsan is usually not administered oftener than once a week in doses of 0.4 gram to 0.5 gram for a course of eight injections.\*

In cases treated only intravenously, lumbar puncture is performed at least once, preferably twice during each course of treatment, to determine the condition of the fluid. As stated above, where the fluid persists in giving a positive reaction in spite of repeated treatments, periodical withdrawal of fluid to increase the permeability of the choroid plexus to the drug circulating in the blood stream may be tried. The fluid withdrawn may, if desired, be replaced by serum or saline. Where the spinal fluid gives a negative reaction, lumbar puncture need not be done unless, of

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\*Where neosalvarsan is used (or novarsenobenzol-Billon) one-third larger dose in every instance is given.

course, there are new or increased symptoms. In the majority of our cases intraspinal treatment was not necessary and in most cases where the intravenous therapy properly carried out was a failure, intraspinal treatment was also unsuccessful.

It must be emphasized that some treatment should be persisted in after the initial few months of more or less intensive therapy for at least one to two years with increasingly greater intervals between treatments. Treatments should not be suspended abruptly and permanently even in the complete absence of symptoms in any type of syphilitic nervous involvement. After the cessation of active symptoms the patients should report once or twice a year for observation and further treatment. It should be kept in mind that besides the lesion of the nervous system, many of these patients are also the victims of syphilitic aortitis, myocarditis, endarteritis, etc., and should for this reason also be treated. In the present status of the subject it can conservatively be stated that a life-long observation and control of the patient not only from the clinical but also from the serobiological standpoint is desirable and essential.

*Group III.*—In another large group we place cases of more advanced tabes dorsalis, late cerebrospinal lues, optic nerve atrophies, spastic paraplegia, and chronic syphilitic epilepsy. In many of these patients there are destructive lesions involving one or more extremities and in some pains and crises are still predominating factors. We can frequently accomplish the gradual abolition of the pain and the occasional disappearance of the crises. Girdle sensations and paresthesias or anesthetics are not often totally or even partially cured. Optic atrophy can not be cured; it can occasionally be arrested, as in Case 12; for how long, we are as yet unable to say, but we have not seen any cases where careful and conservative treatment has caused the lesion to progress any faster than before treatment was begun. In this group of cases ataxia is often a marked symptom, and our experience teaches that by means of intravenous therapy, with the aid of reeducational and other local measures, much can be accomplished to make the patient self-reliant. The more advanced the lesion and the more marked the loss of station, the more essential the mechanical features of the treatment, as in Case 13.

In the treatment of the ataxia of the tabetic and cerebrospinal luetic insofar as it interferes with his gait, we must reeducate his muscle sense and abolish his sense of fear. The method introduced by Maloney<sup>36</sup> is best suited to this purpose.

It is our practice in this group to administer salvarsan intravenously every two weeks, occasionally every week, in doses of 0.4 to 0.5 gram for a period of two or three months, and follow it by inunctions or injections of mercury. At the same time the reeducational measures should be carried out. Where ataxia is marked, mercurial injections should be given with great care. Often a painful injection may set the patient back for weeks. In such cases inunctions are far better. A course of thirty rubbings is given by a competent masseur in a warm room with the windows closed. The course of treatment is repeated once or twice a year until the symptoms are ameliorated. If the pain resists the treatment described, the patient may be punctured once or twice a month, the spinal fluid being withdrawn until the fluid almost ceases to flow, and 15 to 20 c.c. normal inactivated serum introduced. In these cases, if desired, medicated fluid, such as salvarsanized serum, may be used, though we believe it has no advantage. This treatment should not be persisted in if the reaction is severe. In cases with positive biological findings in the fluid the above procedures usually result in a diminution of the cell count and globulin reaction, and occasionally the Wassermann becomes negative. In cases with impotence, improvement may possibly follow this procedure, or as in a few cases treated by us by lumbar puncture followed by the introduction and removal of 20 c.c. of saline (saline lavage of the canal) twice or oftener. The cure of impotence is, however, unusual.

Bladder disturbances occur in all forms of nervous syphilis. There are various degrees of retention and incontinence. Examination should be made in every case to determine the exact degree of bladder control. The ability of the patient to retain his urine many hours is often the earliest sign of retention; if allowed to continue, atony of the bladder may occur. Therefore the patient should be instructed to urinate at least once every three or four hours. Weakness of the bladder with dribbling of urine at times may be helped by the occasional passage of sounds and instillation

of silver nitrate  $\frac{1}{2}$  per cent to 1 per cent into the posterior urethra. The rationale of this therapy is unknown. Faradism, by means of rectal or urethral electrodes and the high frequency current may also be tried to tone up the detrusor and sphincter muscles. When retention is complete and if there is dribbling from overflow incontinence, catheterization under aseptic precautions is of course necessary.

In the treatment of diseases of the nervous system patience is indeed a virtue. Constant attention to details, the continuation of treatment until improvement is apparent, within reasonable limits, a display of sympathy for the patient and an attitude of optimism are great factors leading to success.\* In perhaps no type of disease is the psychologic effect so great as in tabes, where encouragement helps to abolish fear, which is a great factor in retarding independent locomotion. Indeed, so susceptible is the tabetic to the psychologic influence of new and possibly helpful procedures that he is apt to exaggerate the benefit derived therefrom. This fact is to be borne in mind in attributing too great weight to the bald statements of patients concerning the effect of treatment of one kind or another.

#### TREATMENT OF GENERAL PARESIS

Owing to the uniformly fatal prognosis warranted in patients in whom the diagnosis of general paresis is definitely established, it is of the greatest importance to avail ourselves of every possible means of arriving at a diagnosis, if this can be done, in the preparetic or prepsychotic stage, at which time the early prodromal symptoms of neurasthenia and psychasthenia manifest themselves. It is a period in the evolution of the luetic nervous process in which an individual with suspicious physical signs presents none of the definite signs of mental deterioration characteristic of the true parietic, but in whom there are certain persistent biological phenomena characteristic of paresis; viz., positive Wassermann reactions in the blood and spinal fluid, increase in the globulin content and pleocytosis of the spinal fluid, and a "paretic"

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\*Treatment should be so directed that the patient's general condition is benefited. If intensive treatment is not well borne, the patient should be given a rest and attention paid to the task of improving the symptoms and bettering the general condition. If treatment can not be pushed as indicated, less frequent treatment over long periods of time even at great intervals often gives remarkable results, as in Case 14.



curve with the gold solution reaction in the fluid which is almost constantly found in this disease. Our pathologic knowledge is insufficient to enable us to say whether at this period in the progress of the disease, before the manifestation of psychic degeneration, the syphilitic individual just characterized does not already present the profound brain lesions of general paresis. Lesions characteristic of general paresis have been found in cases of syphilis presenting none of the clinical characteristics of this disease by Warthin<sup>79</sup> and it would seem that there are borderland cases pathologically as well as clinically. Therefore, we deem it prudent to regard all such suspicious patients as potentially parietic and to treat them as intensively as possible in the hope of entirely preventing or materially retarding the full development of the disease. Spirochetes have been demonstrated in a number of cases in the brain in isolated groups or scattered in small groups through the cortex, and it is conceivable that intensive treatment, if applied at the time the organisms show a tendency to multiply, might succeed in preventing their further development if not in destroying them entirely. However, treatment must be instituted before neuronal degeneration is advanced, if the profound intellectual deterioration characteristic of the disease is to be avoided. How often such abortion of the disease can be accomplished, if it can be accomplished at all, we can not say. Once the disease is definitely established clinically in any of its various phases, all authorities are in accord as to the impossibility of bringing about a cure, for at this time there is already a profound degree of cerebral degeneration. Hence the importance of laying great stress on the fact that all individuals with persistently positive biological reactions, with or without involvement of the nervous system, inasmuch as they may come in the category of the potentially parietic class, should never be discharged entirely from observation, but after receiving an initial course of intensive treatment, as advised in Group I, should return for periodic treatment of a less intensive kind as advised in Group III. It is our aim by means of early recognition and prompt treatment of the syphilitic infection (constitutional) and by careful scrutiny of the patient for clinical symptoms referable to the nervous system, especially pupillary changes, and of the spinal fluid for the earliest signs of involve-

ment, coupled with persistent and intensive periodic treatment of all individuals showing a persistence of either clinical or biological phenomena, to reduce the incidence of general paresis. Only the future can tell to what degree we shall succeed.

Inasmuch as there is a unanimity of opinion concerning the incurability of the disease once it is established, can we succeed by means of treatment of any kind or degree in materially prolonging the natural remissions of the disease or in so altering the course of paresis as to make remissions of greater frequency? It is our opinion that so far as the use of salvarsan is concerned, we are not in a position to make a definite statement at this time, in view of the paucity of data at hand and especially because of the rather short period of observation since the introduction of the drug. It is well to bear in mind the fact that general paresis is not a stereotyped disease with a definite unvarying course, but that there are various types of the malady, some of which are more or less rapidly fatal without the occurrence of remissions, as, for example, the excited, the demented, and the markedly depressed types, while other types of the disease are characterized by long intervals of lucidity even without treatment of any kind. In some of our cases it seemed that the institution of treatment was directly responsible for the prompt occurrence of a remission, (Cases 15 and 16) and we have observed patients for more than two years, without a sign of relapse, while in others apparently of no greater initial severity, treatment was ineffective in bringing about much improvement.

Within comparatively recent years the use of sodium nucleinate by hypodermatic injection as introduced by Donath<sup>80</sup> and of tuberculin and other bacterial vaccines as used by v. Wagner von Jauregg caused frequent and often prolonged remissions in paresis including changes in the biological reactions. Indeed, the statistics quoted by Pilz after tuberculin injections compare very favorably with those presented in favor of the intraspinal and intracranial administration of salvarsanized serum. Mott's<sup>81</sup> criticism of the so-called beneficial results from the use of sodium nucleinate applies equally well to the statements of such workers as Cotton,<sup>82</sup> Riggs, Fordyce et alia, viz: "Whenever a new treatment has been adopted for general paralysis and whenever temporary improvement

has been reported in some cases we have always to remember that without any special treatment beyond improving the general health and habits of the patient remission of symptoms and comparative cures occur. It is difficult therefore to separate cause from coincidence \* \* \* \*." Indeed many former enthusiasts of the intraspinal method of treatment of paresis are now giving up the method which they declare is inefficient, for the more radical intracranial methods, which after trial on a rather inadequate material and with too brief a lapse of time, they state tends to eradicate the spirochetes and clear up the symptoms. From what we have learned of the effect of intraventricular treatment on the course of general paresis, we do not hesitate to predict the abandonment of this and similar forms of treatment after a more protracted period of experimentation. While the number of cases of paresis under our care has been limited, from our own experience and from what we can glean from the literature, nothing is to be gained by subjecting these patients to the additional discomforts and expense of prolonged intraspinal therapy, while all forms of intraventricular or intradural therapy are to be unhesitatingly condemned because they offer no greater hope if as great a hope of cure as the more conservative methods. We believe that whenever and wherever temporary improvement has followed such treatment it has in all probability been due either to a natural remission or to the coincidental intravenous therapy, plus the effect of spinal fluid drainage.

In a few of our cases treated intensively (intravenously) it seemed that there was an initial improvement followed by a rapid deterioration, as if the marked destruction of organisms caused such a degree of endotoxin liberation as to overwhelm the individual, causing his death as if by a profound intoxication. On the other hand, we have observed in some cases that during the period of its administration our therapy has had apparently no effect on the clinical condition of the patient, but that within a few weeks of the cessation of treatment there was a marked and rapid improvement. We have noted this tardy or delayed improvement in other syphilitic conditions less frequently perhaps.

The form of therapy to be employed in paresis should be the intensive intravenous injections of arsphenamine as in Group I. Where mental symptoms are marked, lumbar puncture should be done.

the fluid being withdrawn every week or two until the pressure is normal or until the fluid flows from the needle drop by drop especially if the fluid is under great pressure and provided the patient is benefited thereby. From 20 to 50 c.c. of fluid can be removed with safety under the circumstances.

Our experience in the treatment of dementia paralytica has caused us to ponder seriously over the question as to whether the results accomplished in the great majority of cases warrant our subjecting the patient to prolonged intensive treatment in an attempt to bring about a remission. Natural or spontaneous remissions are common in the types of the disease in which our therapy brings about improvement, while in the rapidly fatal and terminal cases treatment is futile. Are we justified from a sociologic and economic standpoint in attempting to restore the true general paretic even of the favorable milder type for a limited period, knowing that complete remissions are rarely of longer duration than a year or two, and often not as long as this? Of course, there is always the possibility that in the very early stages of the disease there may be considerable doubt as to the diagnosis. We may be dealing with a case of diffuse cerebral lues, or with the so-called pseudoparetic type, or with a case of tabes with marked mental symptoms. Often the diagnosis remains in doubt until the subjective improvement from treatment together with a more or less rapid decline in all the biological phenomena makes it clear that the case was not one of true paresis. It is certain then that in the very early stages of the disease when our diagnosis is merely tentative, we must proceed with the most intensive therapy at our command. Nonne,<sup>37</sup> Jacob and Kafka,<sup>37a</sup> Mott<sup>38</sup> and others have shown that cases which were considered dementia paralytica were proved at autopsy to be cases of cerebral lues. Further, there can be no doubt that in an individual gaining his livelihood through efforts not entailing the use to any extent of the intellectual faculties, the production of a remission or of a series of remissions enabling him to support himself and his dependents for a period of months or even a number of years is of considerable importance. Where the patient must maintain his status in society through the exercise of those faculties which are profoundly and progressively involved in paresis, the question of permitting

him to resume his normal life during the period of remission is one that is not so lightly settled. We are not considering the problem of bringing about a remission or prolonging it, accepting for the sake of argument that our treatment can definitely accomplish this, and thereby prolong the life of the individual, but of bringing about such a period of more or less intellectual restoration with almost an absolute certainty that the patient may at any moment become a menace to himself and to society. It is our opinion that during the period of remission the vast majority of paretics are not quite normal. Of great importance is the fact that the judgment is very often impaired, affecting decisions in their social and business life, often with unfortunate results. The memory, too, is rarely unaffected, while the alteration in affectivity, resulting in changes in conduct, especially in their regard for the conventionalities and concerning the moral sense, may bring to the patients and to their family such dire results as to lead us to question the advisability of permitting such individuals to assume the responsibility of their own acts, once the diagnosis is established. Those of us who have the responsibility of guiding the destiny of the unfortunate parietic must not delude ourselves into believing that we have at our command today a means of restoring such an individual to complete competence or of preventing the commission of some overt act that may entail serious consequences at any time; and therefore as physicians it is our duty by legal and other restrictive measures to limit his sphere of activities.

#### PRECAUTIONS AND CARE DURING TREATMENT

There are very few contraindications to the use of arsphenamine and mercury in the treatment of syphilis. Terminal conditions of any kind, senility, and severe organic disease contraindicate the use of arsphenamine except in very small doses, unless the eliminative organs are sufficiently active to excrete the drug. Optic neuritis is not a contraindication to the use of the drug. Optic atrophy is not necessarily a contraindication. If the condition is progressive, and if vision is almost gone, arsphenamine should not be given without acquainting the patient with the possibility of further progression of the lesion despite treatment. Under these circumstances the drug must be administered with the greatest care, beginning

with 0.1 to 0.15 gram or preferably with neoarsphenamine 0.3 gram. A careful ophthalmologic control of the lesion and study of the visual field should be made repeatedly during the course of treatment. The same precautions are essential if there is choking of the disks, and if this condition is extreme and progressive, over three to five diopters, cranial decompression should be performed if treatment is not rapidly beneficial. Cardiovascular conditions, especially if accompanied by high blood pressure, and renal involvement constitute a group of cases frequently met with in sufferers from neurosyphilis requiring the greatest care in the dosage and frequency of treatment. In these conditions and also in all others met with in the patients under consideration, the prime determining factor concerning the possibility of arsphenamine treatment is the integrity of the kidneys.

Before beginning treatment a twenty-four hour specimen of urine should be carefully examined. If this shows the absence of albumin and casts, treatment may be begun. Reexaminations should be made at least once a week, and in case of very intensive treatment, oftener. The appearance of albumin or casts should cause the suspension of active treatment until the urine has cleared up, which will usually occur within a week. If the initial examination of the patient's urine disclosed a nephritic condition, or in the event of the development of renal complications during treatment in addition to the routine examination of the urine, the functional excretory powers of the kidneys should be determined by means of the phenolsulphonephthalein tests, and in doubtful cases, where it is imperative to push the treatment, the estimation of the blood urea and the incoagulable nitrogen in the blood should be the determining factors in the case. It is not always necessary to avoid salvarsan therapy because of the presence of a mild nephritis, but where treatment is given, the dosage should be conservative and the frequency of administration of the drug such as to permit elimination of most of the arsenic injected before a second injection is given. In such instances the injection should not be given oftener than once a fortnight. Intensive intravenous treatment can only be ventured in patients in whom the renal function is adequate if one would avoid the toxic action of the drug.

The development of gastrointestinal symptoms, nausea, vomiting, diarrhea, loss of appetite, should at once cause a temporary suspension of treatment. The indications here are for free catharsis by means of saline cathartics and enemata. The treatment should be carefully resumed only after all symptoms have disappeared.

The patient's skin must be carefully observed each day. The first sign of the appearance of a dermatitis, a petechial or herpetic eruption, or an erythema should cause the suspension of treatment and the institution of eliminative measures as in the above complications.

Likewise, a careful observation of the scleræ and skin should be made each day for the initial appearance of jaundice, which also constitutes an imperative sign for the immediate suspension of treatment and beginning of eliminative measures.

If care is taken in the selection of the cases for very intensive treatment and if in doubtful cases the treatment is begun in a conservative manner, complications will rarely occur. During the past few years we have encountered very few instances where treatment could not be successfully carried out, there were practically no severe complications that jeopardized life, and very few of the minor complications, such as erythemas or dermatitis with exfoliation. There has not been an instance of death due directly to the intensive administration of salvarsan in our service.

However, if complications are to be avoided, the treatment must be carried out as indicated in our schedule, the elimination of the drug by way of the skin, intestinal canal, and kidneys should be enhanced by attention to the eliminative functions of these parts. When a patient is receiving very intensive treatment attention to these essential matters, we repeat, is imperative.

In conjunction with the factors noted above the patient's general condition should be used as a guide as to how well the treatment is being borne. If treatment is not well tolerated, if reactions are frequent, and if the patient is losing ground, it is well to stop treatment, give the patient a vacation and build up the general condition before continuing.

#### HYPERSENSITIVENESS TO ARSPHENAMINE

There remains a consideration of those patients who, after repeated injections of arsphenamine, seem to become hypersensitive

to the drug and in whom the symptoms of vasomotor disturbances are more or less manifested during the injection. We have observed this reaction in few instances during the first injection, but in most cases the symptoms do not occur until two or more injections have been given. The phenomenon, on account of its occurrence after the patient has been "sensitized" by previous injections, the subsequent injection acting as the intoxicating dose, resembles anaphylaxis, but in our opinion the reactions are due to the toxic action of the drug on the vasomotor system. The symptoms vary from a mild dilatation of the vessels of the face causing a slight blushing all the way to severe vasomotor paralytic symptoms with initial dilatation of the superficial vessels of the entire body, accompanied by respiratory difficulty due to extreme dilatation of the vessels of the mucous membranes of the throat, larynx, trachea, and possibly bronchial tubes, with swelling of the tongue and edema of the face. These symptoms may become alarming, the patient rapidly passing from the stage of vasomotor dilatation to the reverse condition, with extreme pallor or cyanosis, cold, clammy skin, pain over the cardiac region, increase of intestinal peristalsis with cramps in the abdomen, and even collapse. The cardiac action is increased, there may be palpitation and in the extreme cases the pulse may become very weak. In one instance in which the reaction occurred after the eighth injection, and in which mild anaphylactoid symptoms had been disregarded in the previous injection, the patient passed into a state of collapse which required heroic action over a period of four hours before the cardiac action was properly restored. This case is mentioned in order to point out the necessity for watching for the first signs of the anaphylactoid reaction, which consist in a slight dilatation of the vessels of the conjunctivæ or skin, with a feeling of warmth in the face, a tickling in the throat or desire to cough, slight abdominal "rumblings" or cramps, or a feeling of slight fullness in the head or difficulty in drawing a deep breath. These signs should cause an immediate suspension of the injection, without withdrawing the needle from the vein. If the symptoms are progressive, the injection should be stopped for the day. If they pass over rapidly, a few more cubic centimeters of the solution may be allowed to pass into the blood and if there are



then no further symptoms the full injection may be given. The phenomena above described may be controlled by the injection of 10 or 15 minims of 1:1000 solution of adrenalin subcutaneously (never intravenously) or of 1/100 of a grain of atropine sulphate, preferably the former. On the subsequent injection of the drug the patient should receive this treatment as a prophylactic ten to fifteen minutes before arsphenamine is given. The injection may then be proceeded with, watching carefully for the appearance of the first signs of the anaphylactoid reaction. In this manner it will be found possible in a large measure to overcome the reactions. After a number of injections of adrenalin a number of the patients who were sensitive to arsphenamine lost their "hypersensitiveness" and could be injected with impunity. In the case cited above in whom the very urgent symptoms arose during an injection, the patient subsequently received more than twenty injections of the drug without untoward incident. Where the patient seems to retain the susceptibility it is wise to suspend the injection of the particular preparation in use for a while and after the rest period to begin with some other preparation of the drug. We have noted reactions of this type following all the various forms of arsphenamine or neoarsphenamine; the reactions occur in nonsyphilitic as well as syphilitic individuals.

In the use of mercury the usual precautions following this drug should be taken to avoid the symptoms of mercurialization and renal irritation.

#### INTRASPINAL MEDICATION

The introduction of arsphenamine and neoarsphenamine as anti-syphilitics was soon followed by attempts on the part of numerous investigators both in this country and abroad to introduce these remedies into the spinal canal in order more directly to influence the syphilitic infection in the nervous system. A number of factors were responsible for this conception, not the least being the rather unsatisfactory results hitherto obtained in the treatment of certain types of nervous syphilis. It was also found that in some cases the blood Wassermann reaction was completely negative or became negative after treatment, while the spinal fluid showed definite biological evidence of changes believed to be due

to localization of the infection in the nervous system. It was repeatedly asserted that remedies applied intravenously, intramuscularly, or in any of the usual ways, failed to reach the spinal fluid, due to the impermeability of the secretory apparatus, and hence did not reach the foci of infection in the nervous system. In further support of this statement certain experiments were adduced purporting to show that dyestuffs injected intravenously failed to stain the cells of the cerebrospinal system, while the same drugs, injected intraspinally, caused diffuse staining of these tissues. It was also pointed out that experience with the intraspinal treatment of such diseases as epidemic cerebrospinal meningitis (Flexner<sup>39</sup>), pneumococcus meningitis (Lamar<sup>40</sup>), influenzal meningitis (Wollstein<sup>41</sup>), and in poliomyelitis (Flexner and Amoss<sup>42</sup>), "demonstrated that such diseases can not be controlled except by subarachnoid therapy," and that "syphilitic meningo-encephalitis and meningomyelitis differed in no way from other diseases of these parts insofar as the method of treatment to be employed was concerned," (Ogilvie<sup>43</sup>).

#### METHODS AND RATIONALE—CRITICAL REVIEW

We shall enter into a brief discussion of the rationale of intraspinal therapy, approaching the problem not only from a physiologic and pathologic standpoint, but also from a clinical standpoint. We shall attempt to point out what merit it has, and what the indications are for the use of the various forms of intraspinal medication in the treatment of syphilis of the nervous system.

There are several methods of intraspinal treatment, and medicaments are introduced into the spinal fluid in a number of different forms. In Europe Marinesco and Minea,<sup>44</sup> Wechselmann,<sup>45</sup> Beriel,<sup>46</sup> Verne and Block,<sup>47</sup> Marie and Levaditi,<sup>48</sup> Ravaut,<sup>49</sup> Gennerich,<sup>50</sup> and others introduced the drug (salvarsan or neosalvarsan) directly into the spinal fluid, although the dosage of the drug and the dilutions of the solutions injected varied greatly. Marinesco and Minea used the patient's serum which they inactivated and to which they added a small amount of neosalvarsan. Ravaut was one of the first to introduce neosalvarsan directly into the spinal fluid. In this country the pioneers were Swift and Ellis.<sup>51</sup> They took into cognizance the irritating and toxic action of sal-

varsan and neosalvarsan when injected intraspinally, especially if the dose injected was more than a fractional one. On the basis of experimental work in animals in which they attempted to show that the serum of such animals previously injected with proper amounts of arsphenamine intravenously and inactivated at 56° C. was spirocheticidal in vitro, they suggested the use of serum obtained from patients three-quarters of an hour after intravenous injections of arsphenamine for intraspinal use. Patients were injected with arsphenamine as usual, blood withdrawn three-quarters of an hour afterwards, allowed to clot, the serum removed either by permitting the blood to stand for a sufficient length of time or by centrifugalization incubated at 37° C. for 45 minutes, and then inactivated in a water bath at 56° C. for thirty minutes. This serum was injected intraspinally in doses of 15 or 20 c.c. either in 40 or 50 per cent strength or undiluted, every two or three weeks, depending upon the reaction. This method was the basis of a number of modifications, chief among which may be mentioned that of Ogilvie,<sup>43</sup> in which a fractional amount of arsphenamine (less than 0.001 gram) is added to the serum before inactivation. This method is similar to that of Marinesco and Minea in which neoarsphenamine is added to the serum after inactivation. One of the chief advantages claimed for the addition of this fractional amount of arsphenamine to the serum, aside from the fact that the dosage of arsphenamine can be more accurately controlled than in the original Swift-Ellis method, is the belief that in combination with arsphenamine the inactivated serum is more spirocheticidal than if the drug alone is injected. In a recent article Ogilvie<sup>52</sup> states that "to administer salvarsan or neosalvarsan intraspinally is unscientific because they are not *per se* spirocheticidal," and that "they serve to perfect a potent spirocheticidal agent only when in combination with blood serum." These statements will be more critically considered later. More recently Byrnes<sup>53</sup> suggested the use of mercuric chloride in serum for intraspinal use, referring to prior work of Ravaut along similar lines. Byrnes states that "the instability of these complex arsenical preparations," referring to the various methods using salvarsan or salvarsanized serum, "and their irritative and toxic properties makes their direct introduction into the dural sac an extremely hazardous procedure \*

\* \* \* \*." Hence the use of mercurialized serum as a substitute for intraspinal therapy. Hammond and Sharpe<sup>54</sup> advocated the treatment of paresis by the introduction of solutions of neoarsphenamine into the lateral ventricles in an effort more directly to reach the depths of the cortex. They claimed that in the intraspinal method the medicament failed to reach the cortex, that even when injected subdurally none of the drug reached the ventricles, and that solutions introduced in this manner experimentally were rapidly drained out of the cranium. Other methods of intraspinal and intracranial injection based upon the same principles have been devised, but lack of space forbids their consideration.\*

Experience has shown that arsphenamine or neoarsphenamine introduced directly into the spinal fluid is responsible for so great a reaction on the part of the nervous system, even when injected in minimal amounts, that its employment has practically been abandoned. Sachs, Strauss and Kaliski<sup>62</sup> have proved, and it has been substantiated by others, that the salvarsanized serum of Swift and Ellis contains either no arsenic at all or so infinitesimal an amount as to be negligible as a spirocheticidal factor. This leads us to an inquiry into the possibility of the serum *per se* acting by virtue of certain immunologic properties present in the blood of the syphilitic patient or produced by the inactivation of the blood either alone or after the addition of less than a milligram of arsphenamine. In other words, does the serum act by virtue of definite immunologic factors produced in the syphilitic individual in the course of his disease or as a result of injections of arsphenamine (antigen)? It is our belief that it does not so act. There is no definite proof of an immunity in syphilis; the evidence from both a clinical and experimental standpoint tending to prove that there is slight or no immunity. Further, the injection of a chemical agent

\*Cotton and Stevenson<sup>82</sup> claimed that with the original Swift-Ellis method they obtained remissions in 33 per cent of their cases lasting two to four years. They were not satisfied, however, as the results were not permanent and the cases relapsed. They attributed these inefficient results to too small dosage possible by the intraspinal method and to too long intervals between the injections. They also claimed that the medicament is too greatly diluted by mixture with the spinal fluid, that a large amount of the serum is absorbed by the spinal cord, and that adhesions at the base may prevent the serum from reaching the cortex. They therefore adopted the method of Wardner by which a trephine opening is made in the skull and the medicated serum introduced under the dura. For this more radical procedure Cotton now makes more or less extravagant claims, but we venture to predict that he will eventually abandon it as he did the intraspinal method in paresis. In the method of Hammond and Sharpe the serum is introduced into the ventricles.

shortly before the withdrawal of the blood can not, surely, give rise to any immune bodies. Does the addition of a fractional amount of salvarsan to the serum before inactivation render the serum more actively treponemocidal? We do not think it does *in vivo*. It is not necessarily true that because the serum is more or less toxic for trypanosomes or for certain spirochetes *in vitro* it has the same action *in vivo*, especially in view of the fact that treponemata in culture lose their virulence rapidly. The same criticism applies to experimental proof of cures in animals, for it is well known that syphilis in animals, especially in rabbits, is spontaneously cured rapidly without treatment, and that even in the presence of lesions containing spirochetes successful inoculations can be brought about.

In a recent communication Kolmer and Toyama have shown that the injection in rabbits of small daily doses of arsphenamine and mercuric chloride failed to increase antibody response to alien corpuscles or typhoid bacilli. On the contrary there was a lowering of antibody production probably due, as they state, to lessening of resistance by toxic effects. As the authors state, such experiments should be done on human serums, as work done on the serums of lower animals may not be a true index in human cases.

Arsphenamine by itself on the other hand is not an indifferent agent, as has been asserted, for the experiments of Noguchi<sup>55</sup> show that both arsphenamine and neoarsphenamine are inimical to the growth of *Treponema pallidum* in concentrations up to 1:7500. This concentration can not be effected in the spinal fluid by the direct or indirect application of the drug, owing to its toxic action on the tissues of the nervous system.

Further, the underlying principle in the treatment of the infectious meningitides by intraspinal therapy is after all not the same, nor are the pathologic conditions similar. In the former we attempt to control a more or less superficial and often localized infection by means of the intraspinal injection of an antiserum, while in syphilis we are dealing with a more or less deep-seated infection, often not localized to the nervous system, in which the superficial inflammation is usually incidental or secondary. In short, in the intraspinal treatment of syphilis of the nervous system as now carried out, we are actually injecting merely an inae-

tivated serum with or without a minimal concentration of salvarsan or mercury.

There now remains a brief consideration of the salient facts concerning the *physiology of the spinal fluid in relation to the mechanism of the secretion of certain drugs from the blood stream into the fluid and of the absorption of drugs introduced into the spinal fluid*, especially in relation to the possibility of such medicaments reaching the cells of the nervous system.

It has been asserted repeatedly in support of the intrathecal route that salvarsan can not pass the barrier of the choroid plexus to reach the spinal fluid or the nervous tissue when injected intravenously; hence the direct introduction of the drug into the spinal fluid. The facts available from a study of the physiology of the fluid show that the fluid is not the "lymph" of the brain and spinal cord and does not act as a nutrient medium between the blood and the neurones of the central nervous system, but that it serves as an excretory pathway. The assumption that the spinal fluid is the lymph of the brain and cord is based on the dictum of Mott<sup>56</sup> and of Lewandowsky.<sup>57</sup> According to Halliburton and Dixon<sup>58</sup> the spinal fluid is not an exudation from the blood stream and can not be considered homologous to the body lymph. Its richness in carbon dioxide is evidence of its excretory function. It is a perfect physiologic medium and its function is protective, acting like a cushion or buffer between the brain and cord and the surrounding bony canal and brain vault tending to equalize the pressure in the cerebrospinal cavity. A consideration of the secretion and absorption of the fluid makes it clear that substances introduced into the spinal fluid are very rapidly absorbed into the blood stream. The mechanism is briefly the following one: The spinal fluid is secreted by the appendymal cells of the choroid plexuses into the lateral ventricles, finding its way through the foramina of Monro into the third ventricle, passing through the aqueduct of Sylvius into the fourth ventricle, after which it escapes into the subarachnoid space through the foramina of Magendie and Luschka. The total amount of spinal fluid present in the ventricles and subarachnoid space does not exceed from 100 to 150 c.c. The rate of absorption of the fluid is very rapid, the experiments of Dandy and Blackfan<sup>59</sup> showing that 35 to 60

per cent is reabsorbed into the venous channels within two hours. The chief method of absorption of the fluid, according to Weed,<sup>60</sup> is by filtration through arachnoid villi into the great sinuses in the dura, although there is a possibility of the process being a diffuse one, the venous plexuses of the spinal meninges taking a part.

It is agreed by most investigators that the return of the spinal fluid by way of the so-called pericapillary and perineuronal lymph spaces or sheaths is a very insignificant one. In fact, the use of the term perivascular or perineuronal lymph space is more or less fanciful, in that it suggests that these spaces contain lymph. In the opinion of Weed these sheaths do not contain lymph, nor do they serve to carry nutrition to the tissues. They do, however, carry waste matter from the nervous tissue into the spinal fluid, the direction of the flow, be it noted, being away from the tissues towards the spinal fluid, rather than from the surface towards the cortex or subcortical region. This conception of the perineuronal lymph sheaths is to be borne in mind, especially in conjunction with the statements of the advocates of intraspinal therapy that these sheaths serve as a means of reaching the depths of the nervous tissues when drugs or sera are introduced into the spinal fluid. In the injection experiments of Weed it was not possible to detect dyestuffs injected into the subarachnoid space in these perineuronal or perivascular sheaths under normal conditions. They could be detected only if the brain was rendered anemic, thus causing the spaces to fill up by suction, in order to replace the loss of fluid. The pressure in the cerebral capillaries is greater than in the spinal fluid, leading Weed to state that "since the pressure in the cerebral capillaries is considerably higher than the cerebrospinal tension, far more likely is it that fluid leaves the cerebral capillaries, circulates in the pericapillary and perineuronal spaces, yielding nourishment and receiving waste products, finally leaving the tissues by the pericapillary and perivascular spaces to the subarachnoid cavities over the surface. Thence absorption into the venous channels takes place." Not only does this statement serve as an explanation for failure to reach the nervous tissues by way of the spinal fluid, but it also is evidence in favor of the intravenous route for reaching the cortex through the rich capillary supply of this region. Furthermore,

substances injected into the spinal fluid must be introduced under great pressure to reverse the natural direction of the flow. There have been marked differences in the degree of penetration after experimental intraspinal injections of pigment due in large part to the amount of fluid injected and the pressure under which the material was introduced. For the most part the experiments were conducted in animals under conditions not obtaining during life or on the cadaver, so that the staining of the basal and cortical cells in the experiments was artificial. It is to be doubted if substances injected intraspinally under a pressure and in amounts possible during life reach the cranial subarachnoid. In experiments made postmortem showing diffuse staining of the cortex the conditions are unphysiologic, and probably a mere diffuse coloring of the cells not the result of metabolic assimilation. As Schoenberg<sup>61</sup> pointed out, the introduction of pigment into the lumbar region by intraspinal injection stained only the spinal subarachnoid, failing to reach the cortex at all. It is known that the diffusion process is very slow in the lower spinal region, the site chosen for intraspinal injections. The experiments of Hammond and Sharpe showed that trypan blue injected subdurally diffused to a slight degree and very slowly. After they introduced the dye into the ventricle it extended down only as far as the mid-cervical region in an hour. In the subcerebellar region the diffusion was very rapid. With the rapid rate of absorption of the spinal fluid, as pointed out, substances introduced into the spinal fluid are rapidly reabsorbed into the blood stream, and if introduced in the lumbar region, are probably not diffused to any great extent if at all beyond the site of injection. This belief is strengthened by the lack of proof of a current of flow of spinal fluid from below upward and in the reverse direction, although there is probably some movement of the fluid with respiration.

It is relevant at this point to consider whether salvarsan reaches the nervous tissue when injected intravenously. The fact that arsenic has not been found in the spinal fluid by some investigators after intravenous injections has led many to the acceptance of the statement that the drug does not penetrate the nervous tissues when so administered. McIntosh and Fildes were unable to find arsenic in the brain of a normal rabbit after the



injection of arsphenamine and neoarsphenamine intravenously, but it must be borne in mind that we are not dealing with normal individuals when treating cases of nervous syphilis. In most instances not only the vessels but also the coverings of the brain and cord and the nervous tissues of these patients show pathologic change. It has been demonstrated by Ullman<sup>63</sup> that more arsenic is found in diseased tissues than in normal tissues after the injection of this drug. This has been found to apply also to the iodides by Loeb<sup>64</sup> and others. The experiments of Tilney and Woolsey,<sup>65</sup> who injected trypan blue both intravenously and intraspinally, have also been used as arguments against the intravenous route for the injection of arsenicals as a means of reaching the nervous tissues. By means of these experiments they attempted to prove that the drug injected intravenously did not reach the cortical cells and interior of the brain as well as when it was injected intraspinally. As we have already pointed out, the abnormal conditions under which these experiments were carried out serve in great measure to nullify their value. Recently, however, McIntosh and Fildes have demonstrated that such dyestuffs as methylene blue and neutral red stain the entire brain and cord when injected intravenously, and they have shown that the penetration of these organs by dyes seems to depend upon the easy solubility of the substance in water and chloroform. Presumably this applies also to the drugs used in our therapy, so that the hope of the future for the more successful eradication of syphilitic infection of the nervous system would seem to lie in the discovery of a treponemicidal remedy as readily soluble as the above dyes, able to reach the innermost depths of the nervous tissue, without acting in a toxic manner.

#### SECRETION OF ARSPHENAMINE BY CHOROID PLEXUS

The statement that drugs administered intravenously do not reach the spinal fluid on account of the selective secreting activity of the choroid plexus must also be subjected to a closer and more critical analysis. In a previous communication we stated that in patients suffering from syphilis of the nervous system arsenic made its appearance in the spinal fluid after the intravenous injection of salvarsan. This statement was based upon an analy-

sis of a number of spinal fluids made for us by Benedict<sup>66</sup> and by Kuttner<sup>67</sup> independently, the fluids being withdrawn within twenty-four hours of the intravenous injection. The amount of salvarsan injected intravenously was about 0.3-0.4 gram and the amount recovered from the fluid was about one-sixth to one-tenth the content of the whole blood after such injection. We have calculated on the basis of body weight and blood volume that immediately after the administration of salvarsan (0.4 gram) before the drug is fixed by the body cells each cubic centimeter of blood contains 0.0001 gram of arsphenamine or 0.000033 gram of metallic arsenic. Within forty-five minutes after intravenous injection of salvarsan the blood is found to contain an infinitesimal trace or absolutely none of the drug, due to the anchoring of the drug by the tissue cells. Benedict found 0.000002 gram for each cubic centimeter in a few instances and never more than 0.000005 gram per cubic centimeter. The minimal amount recovered from the spinal fluid after intravenous injection was 0.00001 gram of arsphenamine, the maximal amount 0.000016 gram. Allowing for a certain amount of variation in the amount secreted into the spinal fluid, it will be seen that the amount in the fluid exceeds that which is occasionally present in the blood one hour after intravenous injection. Further, in the modifications of the Swift-Ellis intraspinal method not more than one-third to two-thirds of a milligram (0.0003 to 0.0006 gram) of arsphenamine can be safely added to the serum to be given intraspinally. The total quantity of fluid present in the average patient varies from say 75 c.c. to 150 c.c., which represents on a basis of say 100 c.c. of spinal fluid a dilution of 0.000005 gram of arsphenamine. *Thus it will be seen that the amount of salvarsan present in the spinal fluid after intravenous injection exceeds that which can safely be introduced into the fluid in serum or otherwise.* Barbat<sup>68</sup> found that about four-fifths of the arsenic is fixed in the body cells one hour after intravenous injection, leaving one-fifth in the blood, a proportion he stated of 1:100000. In the spinal fluid which was drawn twenty-four hours after injection intravenously arsenic was found from a trace to ten per million, the average being one-fourth per million. In a recent article Barbat<sup>68a</sup> states that after intravenous injection of arsphenamine arsenic was found in the spinal fluid

within twenty-four hours in twenty-five out of twenty-six cases studied, and that in eighteen out of twenty-six cases the arsenic was found in the spinal fluid shortly after the intravenous injection.\* In a similar study instituted soon after the appearance of this paper Kuttner and one of us (Kaliski<sup>69</sup>) have been able to confirm this work in a number of cases. This investigation is still in progress and the results will be reported later.

Rieger and Solomon<sup>75</sup> examined the spinal fluids of 123 neurosyphilitic patients collected at arbitrary intervals after intravenous injections of from 0.3 to 0.6 gram arsphenamine by a refinement of the Marsh technic which enabled them to detect by a characteristic mirror a micromilligram of arsenious oxide. Of these 123 cases "the arsenic content of thirty-nine became appreciable within one or two hours." As they say "whether the fluids found negative were so because their arsenic content at the time of collection had not reached the limits of delicacy of the analytic method or because they had already depreciated therefrom, can not be stated. Also because of the few samples collected at intervals beyond two hours, it can not be concluded from these data that no arsphenamine passes into the cerebrospinal fluid after the second hour or that it does not remain there in appreciable amounts for periods longer than one hour." They believe that the arsphenamine concentration of the cerebrospinal fluid attains its maximum during the first hour.

In view of these facts we believe that the commonly accepted statements that the choroid plexus and meninges in cases of neurosyphilis are impermeable to the passage of drugs and that arsenic (arsphenamine) introduced intravenously does not reach the spinal fluid are erroneous. *Arsphenamine reaches the fluid in detectable amounts, not only equal to but greater than what can be given intraspinally, and also reaches the nervous tissue wherever this tissue is supplied by blood vessels.* We are not yet in a position to state whether arsenic regularly reaches the fluid or tissues in normal cases. What the mechanism is that causes the choroid plexus and meninges to become permeable in neurosyphilis we can only conjecture. Where there is an inflammatory

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\*These chemical analyses for arsenic were made for Barbat in the Hygienic Laboratory at Washington.

reaction in the meninges, as in the various meningitides, the spinal fluid is permeable to antibodies circulating in the blood stream. Intraspinal injections of human serum, homologous or autogenous or medicated serum, of normal saline solution, or of a foreign serum, as horse serum, cause a certain amount of reaction on the part of the meninges (serositis) and possibly of the choroid plexus (ependymitis), which then become more or less permeable. In general paresis the meninges are permeable for hemolytic amboceptors (Weil and Kafka<sup>70</sup>).

Kolmer and Sekiguchi<sup>76</sup> have contributed important evidence tending to show that the spinal fluid contains antibodies elaborated by the organism or developed as a result of active or passive immunization. They showed that the removal of blood from normal dogs, followed by intravenous injections of human syphilitic serum (from 30 to 50 c.c. per kilo of body weight) caused small amount of syphilitic reagin in the cerebrospinal fluid. This reagin was found in the fluid as early as three hours after the transfusion of syphilitic serum. The amount of reagin found was small. After irritation of the meninges by horse serum, more reagin was found in the cerebrospinal fluid. All traces of the reagin disappeared from the fluid of the dogs within forty-eight hours. Dog typhoid immune serum, injected into a normal dog intravenously, caused traces of agglutinin to appear in the fluid of the dog within three hours; it disappeared within forty-eight hours. It was thus shown that the passage of antibody from the blood to the cerebrospinal fluid is possible, when the antibody exists in the blood in a high state of concentration. In human syphilis the reagin may pass from the blood, but its presence in the spinal fluid generally indicates the presence and activity of *Spirochete pallida* in the organs of the nervous system.

Mestrezat and Sappey<sup>71</sup> state that the injection of electromercuriol intraspinally causes a meningitis which renders the membranes permeable to the passage of antibodies and drugs into the canal (quoted by Barbat<sup>72</sup>). Barbat believes that the reduction of the intraspinal pressure by withdrawal of large amounts of spinal fluid also increases the permeability of the meninges by the causation of a congestion, the dilated capillaries permitting the passage of their contents with greater freedom. In intraspinal

medication, or after lumbar puncture, all of the above factors obtain to a certain degree. In the various types of syphilis of the nervous system there is a certain amount of alteration in the meninges in a fair proportion of the cases. The withdrawal of spinal fluid preliminary to intraspinal medication reduces the pressure in the canal and very probably creates a certain amount of congestion in the meninges and in the choroid plexus. The introduction of the medicated fluid is more or less irritating, accounting for further congestion if not inflammation of the secreting glands and meninges. In view of the fact that the serum injected contains either no salvarsan at all, as in the Swift-Ellis method, or too insignificant a trace to be of therapeutic value *per se* (as in the Ogilvie modification), and inasmuch as we have pointed out that similar changes in the biological reaction can be brought about by the use of nonmedicated serum or by repeated lumbar puncture, and further, in view of the fact that intraspinal medication has usually been accompanied by intravenous therapy, it would seem that the explanation of beneficial results attributed to intrathecal injections lies, not in the intraspinal injection primarily, whatever it may be, but in the increased permeability of the meninges brought about by irritation of the secreting mechanism of the choroid plexus and meninges by the injection secondarily, permitting drugs injected into the blood or substances elaborated by the organism to enter the nervous tissue, and to a lesser degree in the reduction of cerebrospinal fluid tension. This accounts for the fact that clinical improvement as a result of treatment is more frequently brought about and is more marked where the lesion is an exudative one, rich in blood vessels, and less frequent and definite in lesions of a degenerative type, as in true tabes and dementia paralytica.

#### CLINICAL VALUE OF INTRASPINAL THERAPY

We shall now discuss the subject of intraspinal therapy from the practical standpoint on the basis of what it has accomplished for the neurosyphilitic in the way of ameliorating the symptoms of the disease or eradicating the disease process. In the last analysis it must be admitted that the achievement of definite clinical results must bear great weight in deciding the value of this form

of therapy. But in reaching a decision our judgment should be based upon an analysis of a fairly large number and variety of cases. A sufficient length of time should be allowed to elapse before rendering a decision in view of the peculiarity of the course of the disease under treatment, in order to permit of proper perspective in estimating clinical change especially in subjective symptoms. It can not be too forcibly emphasized nor too frequently reiterated that in pathologic conditions in which the course of the disease is essentially chronic and subject to spontaneous arrests and remissions too great weight should not be laid on clinical or laboratory improvement following intraspinal therapy, unless it is of a permanent character and unless the result can be regularly achieved by this form of treatment.

Does intraspinal therapy cure syphilis of the nervous system or does it cause any degree of alteration in the course of the disease or amelioration of the symptoms of the disease? As a result of more than three years' experience with this method in all its various branches and modifications we do not think it is possible to speak of a "cure." So far as we can ascertain, the intraspinal method of treatment alone can not be said to have brought about a single undoubted cure of the disease in any of its forms. According to our own experience a number of cases of cerebrospinal syphilis, especially with marked meningeal exudation, have been definitely improved both clinically and biologically, and possibly cured, by *combined* intravenous and intraspinal therapy as in Case 20. In some of these cases Swift-Ellis's salvarsanized serum or the reinforced serum according to Ogilvie's modification, or patients' nonmedicated serum was used, but in nearly all of these cases intraspinal treatment was combined with the intravenous use of arsphenamine with or without subsequent mercurial therapy. The type of intraspinal injection so far as the curative effect of the serum is concerned, does not seem to be material, for improvement may follow the use of normal serum, as admitted by Swift,<sup>11</sup> as well as medicated serum as in Cases 21 and 22. It should be remembered that numerous cases of this type of syphilis are markedly benefited by intravenous arsphenamine treatment alone as in Cases 23 and 25. Even the old form of "mixed treatment" has caused the arrest if not the cure of cerebrospinal syphilis and tabes,

as in Case 24. So that it has become our opinion that the only indication for the use of intraspinal treatment in cerebrospinal syphilis is in cases of the type here referred to with positive biological reactions in the spinal fluid, where intensive intravenous salvarsan and mercurial therapy as outlined by us has been given a thorough trial and found to be ineffectual in bringing about definite improvement both clinically and biologically within a reasonable length of time, say six months to a year. As we shall show that intraspinal therapy is not infrequently followed by marked discomfort and occasionally is distinctly hazardous to the patient, intravenous injections should always first be resorted to and a period of freedom from treatment after their cessation should be permitted to elapse in order to determine by lumbar puncture whether biological change in the fluid has not occurred before beginning intraspinal therapy. In *tabes dorsalis*, especially in the earlier forms, where improvement after intravenous injections has not been satisfactory and where the reactions in the spinal fluid point to meningeal inflammation or where the Wassermann reaction in the fluid is persistently positive, intraspinal medication may be tried in conjunction with other necessary measures. In late *tabes*, and in all cases with negative spinal fluid reactions, intraspinal medication is meddling therapy, and should not be recommended. In cases of this type, if the spinal fluid is under great pressure, occasional lumbar puncture may be tried and is at times followed by subjective improvement. In *dementia paralytica* we have found intraspinal medication alone to be useless. It does not cure paresis, and it is a question in our minds whether it is directly responsible ever for the more frequent production of remissions or the lengthening of the period of remissions. Intensive intravenous therapy, plus occasional tapping of the spinal canal, will usually bring about the same results, and if such treatment is unsuccessful, other forms of therapy will usually also fail, as in Cases 26 and 27. Intraventricular injections of medicated serum or subdural injections are no more successful than intraspinal therapy and should not be recommended. While we have had no personal experience in the use of these latter methods, from what we have seen of cases treated by others and from published reports, we do not hesitate to speak of the methods as

distinctly heroic and entirely futile in their results. In optic nerve atrophy of the primary type intraspinal medication does not effect a cure, and it is questionable if the condition is at all permanently altered by such treatment, as in Case 12. In the interstitial type the coincident intravenous treatment is probably responsible for whatever improvement is noted in the progress of the lesion. The results of intraventricular injections up to the present time have not been such as to warrant their recommendation in this condition.

Intraspinal medication should always be accompanied by intravenous injections of salvarsan as in the original method of Swift and Ellis. Where medicated sera or normal sera are used intraspinally, intravenous injections of salvarsan should be used alternately with the intraspinal injections. We thus agree with Swift<sup>72</sup> that the intraspinal method should not be used to the exclusion of other methods and our experience leads us also to coincide with his statement that "intraspinal treatment alone is not the best or the ideal treatment of syphilis of the nervous system." Indeed, it has always been our contention that the advocates of the intraspinal method never took sufficiently into consideration the influence of the coincident therapy in bringing about improvement in the disease under treatment, nor were such factors as spontaneous changes in symptoms or biological reactions considered as possible factors, but that because amelioration occurred it was the result of intraspinal medication, *post hoc ergo propter hoc*. In this connection witness the statement of Fordyce<sup>73</sup> who writes that the "logic of results accomplished must always supersede theoretical reasons why they could not occur. I can not convince my patients who have been cured or relieved of their symptoms by intraspinal treatment after failure of intravenous treatment that theoretically it was impossible for such benefit to have taken place. They smile at theory in the light of accomplished results." While no doubt the patients referred to were benefited by the treatment given, in most if not all instances it was by combined intravenous and intraspinal therapy; yet the argument as presented by Fordyce is similar in every respect to that of the Christian Scientists, let us say, in pointing out recoveries as being the result of the practices of this cult. So long as the absolute rationale of intra-



spinal therapy is unknown and inasmuch as coincidental factors in the cases cited were equally likely to have caused the improvement noted, scientific data tending to throw doubt on if not absolutely disprove the spinal fluid as the logical pathway are more than "interesting physiologic observations." Before intraspinal therapy can be accepted as an independent form of treatment it must be shown beyond the shadow of a doubt that it alone is responsible for definite improvement or cure where other treatment has failed. In a small series of cases treated by intraspinal therapy alone we were not able to satisfy ourselves that this treatment was effective. The fact that practically all experienced neurosyphilologists used combined therapy is sufficient proof of the inadequacy of intraspinal therapy.

Intraspinal therapy should not be attempted unless there are definite indications for its use as outlined above, and it should not be persisted in if after a trial of say six to twelve injections definite subjective or objective as well as biological improvement is noted. The choice of serum to be used can not be dogmatically stated, but the original Swift-Ellis serum or simple patient's serum prepared as in this method will be found less irritating than those sera which are reinforced by the addition of a minimal amount of salvarsan or mercury. Intraspinal treatment should be suspended if any irritative symptoms arise and should be abandoned if these recur or if the patient's clinical condition is made worse.

We have given many hundred injections of medicated and non-medicated serum intraspinally and in most instances if either normal serum or medicated serum in which the amount of salvarsan added is not above a half or a third of a milligram is used the symptoms of reaction on the part of the nervous system are slight and usually negligible. However, the response to intraspinal medication is occasionally very severe. Besides the usual symptoms accompanying the withdrawal of fluid from the spinal canal, which need not be gone into here, the response on the part of the nervous system to intraspinal injections may assume grave proportions. The milder symptoms of meningism may be accompanied in some instances by paralyses, usually transient, occasionally permanent. Bladder and rectal control may be disturbed, and in a number of instances is permanent. Even symptoms of collapse and coma

eventuating in death have been reported where the technic of injection has been faultless. The injection of dilute solutions of neoarsphenamine directly into the canal in quantities not exceeding 1.8 to 2.0 milligrams have caused myelitis and death. Draper<sup>74</sup> states that in a series of 355 injections of arsphenamine serum 80 per cent of all patients have pain and 26.4 per cent have reactions from mild pain to a very severe reaction, and he further says: "It is obvious that the intravenous intraspinal method is not devoid of difficulties for the patients \* \* \*. With very many patients there is practically no discomfort worth recording, but in a fair proportion the treatment is distinctly of a heroic nature." This statement is to be contrasted with that of Ogilvie<sup>52</sup> who says that "in more than 3,500 treatments I have seen but one severe reaction of a permanent character follow." Our own experience coincides with that of Draper concerning the reactions following intraspinal therapy even with a faultless technic in a certain number of cases, and in some instances the patient's condition was made worse by the attempts to continue this form of medication, while in rare cases the method is apt to be accompanied by extremely dangerous complications if not a fatal termination.

#### SUMMARY AND CONCLUSIONS

All forms of syphilitic involvement of the central nervous system, including the so-called parasymphilitic diseases, are due to the invasion of the neuraxis and its appendages by the *Treponema pallidum*.

The reaction on the part of the invaded tissue differs markedly in the various clinical types of the disease.

The localization of the disease process is of importance in diagnosis and prognosis, and in the application of therapeutic measures. Foci of disease which are accessible to intravenous and combined therapy may be eradicated by intensive treatment provided the organisms have not become resistant to the drugs now at our command.

Neurons which have been destroyed can not be replaced; and the function of an active physiologic area can not be restored if the destruction has been extensive.

Cerebrospinal syphilis, involving one or all of the structures of the nervous system, is a disease essentially of younger individuals and occurs comparatively soon after infection with syphilis. It is similar

in its pathology to active syphilis elsewhere in the body. There is a great tendency towards involvement of the blood vessels of the neuraxis.

We regard *tabes dorsalis* as a primary neuronie degeneration and differentiate it from *pseudotabes* due to an exudative inflammation of the meninges in the region of the nerve roots and posterior columns. Whether optic atrophy of the tabetic type is always a primary ascending degeneration and analogous to the primary neuronie degeneration of *tabes* or is occasionally due to an exudative or interstitial lesion of the optic nerve is a mooted question.

In *dementia paralytica* the toxic action of the *Treponema pallidum* causes widespread destruction of neurones with an active mesoblastic response. Similar lesions of more circumscribed extent and with a milder degree of reaction have been found in cases clinically not general paresis. Whether these lesions are to be looked upon as forms of cerebral lues or possibly the forerunners of true *dementia paralytica* is as yet doubtful.

Infection of the nervous system occurs by a lighting up dormant foci of *treponemata* within the central nervous system or by invasion of the neuraxis from without probably by the carrying of virulent organisms by the blood from other viscera.

The cerebrospinal fluid does not convey the infecting agent to the nervous system, but in its capacity of carrying waste material from the brain and cord it is secondarily contaminated.

The cerebrospinal fluid should be examined in every case of constitutional syphilis before pronouncing the patient cured even in the absence of subjective and objective symptoms of nervous involvement. This is of importance in view of the possibility of early infection of a latent type as evidenced by positive biological reactions in the spinal fluid even with a negative Wassermann reaction in the blood.

A large percentage of constitutional syphilitics show some abnormality of the spinal fluid in the early stages of the disease although few give physical signs indicative of involvement of the central nervous system. Whether these changes are due to the general syphilitic toxemia or are definitive signs of actual invasion of the neuraxis by the *treponemata* is as yet a mooted question. Most of these patients eventually give normal reactions, but about 12 per cent persist in giving abnormal reactions in the fluid. Inasmuch as this number corresponds closely with the percentage of individuals who eventually

develop nervous syphilis, it seems justifiable to look upon the persistence of abnormal spinal fluid reactions as the earliest sign of invasion of the nervous system by the *Treponema pallidum*.

The presence of a positive Wassermann reaction in the blood means active or latent syphilis. A positive Wassermann reaction in the spinal fluid signifies invasion of the central nervous system. A negative Wassermann reaction in the spinal fluid does not exclude the presence of syphilitic involvement of the nervous system. This is especially true of cerebral endarteritis. A negative Wassermann reaction in the spinal fluid after treatment is not absolute evidence of the subsidence or cure of a once existent lesion. A persistently positive Wassermann reaction in the spinal fluid is not inconsistent with an apparently stationary lesion and clinically arrested case. A negative Wassermann reaction in the blood in the presence of a positive reaction in the fluid does not signify necessarily the localization of the syphilitic lesion to the central nervous system. Most of these patients have in addition to the nervous involvement syphilitic lesions in other viscera of the body and should be treated by intravenous or combined treatment.

It is essential to bear in mind the fact that in all diagnostic, prognostic and therapeutic decisions due weight should be given both to the clinical aspect of the case and to the laboratory data ascertained by an examination of the blood and spinal fluid.

The biological reactions in the spinal fluid are influenced by a number of factors among which may be mentioned treatment by intravenous and combined methods, intraspinal treatment of various forms, repeated lumbar puncture and temperature producing sera, e. g., tuberculin. The reactions may also disappear spontaneously during the course of the disease.

The treatment of constitutional syphilis must be intensive and should be kept up even after the blood Wassermann is negative in order to prevent involvement of the nervous system. If the Wassermann reaction in the blood remains persistently positive, treatment can never be wholly suspended. The same applies if the reaction in the spinal fluid persists.

The methods of treatment of cerebrospinal syphilis, tabes dorsalis, and general paresis and the possibility of a cure of these diseases are discussed in detail.

A plea is made for more intensive intravenous treatment of syphilitic diseases of the central nervous system.

The practice of intraspinal medication is subjected to critical review on theoretic grounds and also from the standpoint of results achieved. The physiology of the spinal fluid is discussed in detail especially in relation to the question of the direct introduction of arsphenamine and medicated sera into the cerebrospinal fluid.

We have proved that arsphenamine and immune bodies pass the barrier of the choroid plexus and appear in the spinal fluid after intravenous therapy. It is shown that after therapeutic doses of arsphenamine intravenously arsenic is found in the spinal fluid in greater concentration than can be effected by the introduction of salvarsanized serum or arsphenamine into the fluid. An explanation is offered for the greater permeability of the choroid plexus to drugs circulating in the blood stream after intraspinal procedures.

Syphilis of the nervous system is best combated by prompt recognition of the disease followed by intensive treatment as outlined in the text. The intensive and prolonged use of arsphenamine intravenously combined with the exhibition of mercury and iodides has given us the best results. Intraspinal medication is of occasional and secondary value only. It may be tried in selected cases after intravenous and combined therapy have proved ineffectual in the event that the biological reactions in the spinal fluid are positive. Reeducational measures are of great value in the treatment of ataxic patients.

The authors wish to express their great indebtedness to Doctor B. Sachs for the privilege of reporting the cases cited in the article and for his helpful advice and sympathetic encouragement during the progress of the work.

## CASE HISTORIES

### CASE 1

F. C., 27 years old, a salesman, admitted to the hospital on September 21, 1916, in a prostrated condition. His past history was quite negative and he denied lues by name or symptom. For more than three months before admission he had been suffering from almost constant, severe headaches, joint and muscle pains, and occasional attacks of fever. For the five days preceding his admission to the hospital the headaches were very much worse and in addition on attempting to take nourishment, vomiting of a violent character ensued. He was extremely nervous and irritable and at times severely prostrated.

*Physical Examination.*—Patient prostrated, face flushed, complaining of headache. Head tender to pressure and percussion. Pupils react to light and accommodation. Hypersensitiveness general. No palsies. Fundi congested (hyperemic), due to increased intracranial pressure. Reflexes normal. No ataxia.

Kernig sign positive. Neck somewhat rigid. Temp. range between normal and 100° F., white blood cells 14750, Polys. 83 per cent.

Lumbar puncture.—550 lymphocytes to c.mm.

Wassermann positive +++++ 0.1 to 1 c.e.

Globulin ++.

Blood Wassermann positive +++++.

1916

Sept. 25.

Status unchanged. Temperature normal. White blood cells 35,000, 86 per cent polys. Received a deep injection of Hg.

Sept. 26. Arsphenamine 0.3 intravenously,

Sept. 28. “ 0.3 “

Sept. 30. “ 0.3 “

Lumbar puncture 500 cells c.mm.

Oct. 1.

Markedly improved. Headache gone.

Kernig and rigidity of neck gone.

Oct. 2.

White Blood Cells 15,300.

Oct. 3.

Slight return of headache.

Oct. 4. Arsphenamine 0.4 intravenously,

Oct. 6.

Lumbar puncture.

Oct. 10. Arsphenamine 0.4 intravenously. Discharged well. Feels fine, able to resume work. Wassermann test has become negative.

Patient returns for treatment October 28, 1916, and between this date and December 8, 1916, he received four injections of arsphenamine intravenously followed by 12 intramuscular injections of Hg salicylate. In addition the iodides were given in 15 drop doses three times a day. At the end of this course of treatment the blood Wassermann reaction was again negative. There were no objective symptoms.

During 1917 two courses of intramuscular injections of Hg salicylate and one injection of salvarsan were administered. Lumbar puncture revealed in November, 1917, an entirely normal spinal fluid. Both blood and spinal fluid in July, 1918, showed negative reactions.

Physical examination revealed nothing abnormal and objectively all reflexes as well as the pupillary reactions were normal. Patient has been at work constantly since his dismissal from hospital in September, 1916.

We regard this case as one of more or less superficial meningeal involvement with positive biological reactions cured by moderately intensive treatment modified after the urgent symptoms had disappeared by the exigencies of the patient's position, that of a traveler.

#### CASE 2

A. J., Feb. 16, 1917, forty years old, musician. One brother and one sister died of paresis. Another brother died of some form of mental disease the exact nature of which is unknown. Denied infection with gonorrhea or syphilis. Has two healthy children. No history of miscarriages. In September, 1910, con-

sulted an oculist who found the right cornea hazy and covered with numerous punctate deposits; a punctate keratitis; and also evidences of a beginning uveitis. Both nerve heads were slightly hazy and indistinct; the veins were very full and the arteries pale. The oculist considered the condition to be luetic. On April 12, 1913, the oculist was consulted again and found that the right cornea had cleared up considerably, the fundus had improved, but there were some deposits on the left cornea. In 1915 he began to show some evidences of mental deterioration but was able to continue at his work until August of that year, when he suffered from a nervous breakdown. At this time had had diplopia for three days. At this time it was also noted that the speech was exalting. He improved somewhat in the next few months but was unable to work because of nervousness and faulty memory. In October, 1916, he had another attack of diplopia and a slight degree of internal strabismus was observed.

At the time of examination his chief complaints were extreme fatigue, marked somnolence, poor memory, irritability, halting speech, and double vision.

*Examination* showed: Very slight paresis of left face and right arm. Paresis of left external rectus, adiadokokinesis of left hand, and incoordination of movements. Reflexes normal.

Pupils reacted to light and accommodation and were equal. Fundi negative. Speech at times incoherent and resembling that of a paretic. Blood Wassermann negative. Spinal fluid Wassermann negative (0.1 to 2 c.c.). Globulin one plus, 500 cells to the c.mm., mostly lymphocytes.

*Diagnosis*.—Cerebral syphilis—congenital. Dementia Paralytica—a possibility.

Between 2/20/17 and 3/5/17 he received 1.6 gm. arsphenamine intravenously. Diplopia and weakness of eye muscle has disappeared. Left facial weakness less evident. Appears much brighter. Speech not so incoherent. For the first two days after treatment was commenced he had been in a state of semistupor, but now even the tendency toward somnolence has disappeared.

*Mar. 15, 1917.* Lumbar puncture. Spinal fluid Wassermann negative, globulin negative, 8 cells per c.mm.

16. Arsphenamine 0.4 intravenous.

27. Mental condition and speech improved. No tendency towards somnolence. He complains of difficulty in focusing on objects and examination shows left pupil larger than right and a slight insufficiency of the right rectus internus muscle.

*Apr. 17.* Arsphenamine 0.4 intravenous. Examination of eyes by Dr. O. Schirmer: Fields normal—Right eye—disc outline not quite normal—slightly blurred—veins wider; probably the beginning of a very low grade papillitis. There appears to be some interference with the conjugate up and down movements. Reaction of pupils normal.

*June 7.* Has taken iodides for past six weeks and there is steady improvement in his condition. His friends, however, still notice his impairment of memory and his lack of concentration. He was examined by the oculist who saw him in 1913 who reported that the uveitis had disappeared but that both optic nerves were hazy, the veins enormously engorged and the arteries moderately engorged. The reaction was sluggish to light and accommodation. He believed the condition was suspicious of tabes dorsalis.

*July 9.* Completed a course of 21 inunctions and has taken twenty-five drops of sodium iodide three times a day. His only complaint is of difficulty in focusing on objects. Gaining in weight.

*Aug. 7.* Arsenobenzol 0.4.

*14.* Noted that the left pupil was again larger than right.

*Nov. 1.* Has been absent from city for six weeks conducting an orchestra. This is the first time in two years that he has been able to do any professional work. His work was not perfectly satisfactory owing to memory defect. On *Nov. 2* there was a return of diplopia which has persisted. Examination showed left K. J. more active than right. Same true of Achilles reflex. Right Babinski. Right pupil larger than left. Insufficiency of right external rectus; slow rotatory nystagmus. Both pupils fixed to light (first time this has been noted); gait somewhat unsteady; drags right leg slightly.

*Nov. 8 to 19.* Arsphenamine 1.6 gm. Pupils show some reaction to strong daylight.

*Nov. 22 to Nov. 26.* Arsphenamine 1.2 gm. intravenous. Pupils react to light (this is the first time in our experience that we have seen the reaction of pupils restored by treatment).

*Nov. 30, 1917, to Jan. 2, 1918.* Arsenobenzol 2.8 gm. intravenously.

*Jan. 2, 1918.* No diplopia—no trouble in focusing. No headaches. Memory much improved. Can remember names and dates. Gait steady. No incoordination in hands. Can now play piano. Has commenced composing music.

*Jan. 9, to Jan. 24.* Arsenobenzol 1.6 gm. intravenously.

*Feb. 20.* Lumbar puncture—sp. fl. Wassermann negative. No cells—blood Wassermann negative.

*June 19.* In the past two months the patient has had a severe attack of erythema nodosum and gastroduodenitis, and yet his mental and physical condition have steadily improved. He is alert, keen, quick in movements and speech. His memory has improved remarkably. He has written the scores for two musical comedies and is under contract to conduct an orchestra.

### CASE 3

J. L., twenty-four years old, single. Was admitted July 30, 1915. Completely paralyzed in all four extremities, which were rigid. He was quite irritable and emotional, crying out from time to time in a peculiar thick, bulbar voice. History of sudden onset on morning of admission, and of severe headache. Later in day patient became somewhat stuporous and head, hands, and feet became rigid and powerless.

*Physical Examination.*—Spontaneous nystagmus. Pupils regular, react to light and accommodation. Extremities all paralyzed and slightly spastic. Exaggeration tendon reflexes. Bilateral ankle clonus and Babinski. Slight left facial; no rigidity head; Kernig doubtful (spasticity). Absent abdominal and cremasterics reflexes.



Blood Wassermann (++++ ) positive. Spinal fluid 0.1 to 1 c.c. ++++ pos.  
26 cells c.mm.,  
+ Globulin.

1915

Aug. 4. Arsphenamine 0.4 intravenously. Condition same as on admission.

Aug. 6. " 0.3 "

Aug. 7. Slight movement right arm, slightly less spastic.

Aug. 9. " 0.3 "

Aug. 11. Diffuse erythema; arsenical. Condition about same. Nephritis.

Aug. 13 to 27. Rash fades. Beginning atrophy muscles arms and legs producing a clinical picture resembling amyotrophic lateral sclerosis. Respirations labored, suggestive of diaphragmatic involvement.

Aug. 27. Arsphenamine 0.2 intravenously. Wassermann ++++; spasticity diminished.

Aug. 31. Wasting of temporals and masseters. Marked jaw jerk. Breathing still bulbar.

Sept. 22. Arsphenamine 0.3 intravenously. Nephritis cleared up, almost.

Sept. 27. " 0.15

Oct. 7. G. C. improved. In wheel chair. Both upper extremities spastic, left greater than right; Exag. wrist and triceps jerks; Lower K. J. exag.; Bilateral inexhaustible clonus; bilateral Babinski; Mentally normal.

Nov. 4. Lumbar puncture. Saline lavage. Still very spastic, but can flex knees somewhat.

Dec. 8. Spasticity increasing under observation. Lower extremities rigid. All reflexes markedly exag. Muscular power increased. Excessive excitability under mechanical stimulation.

Dec. 11. Lumbar puncture. 15 c.c. fluid replaced by 15 c.c. autoserum.

Dec. 13. Arsphenamine 0.3.

Dec. 28. Lumbar puncture. 15 c.c. fluid replaced by 15 c.c. autoserum.

Dec. 30. Out of bed. Feels better.

1916

Jan. 4. Patient feels fine. Status unchanged.

Jan. 14.				<i>Lumbar puncture.</i> Saline lavage. Wassermann four-plus 0.1 to 1 c.c. Globulin plus, 8 cells.
Jan. 21.	Arsphenamine	0.4	intravenously.	
Jan. 28.	"	0.1	"	Became weak during injection.
Feb. 9.	"	0.3	"	
Feb. 16.	"	0.35	"	
Feb. 23.	"	0.4	"	
Feb. 27.				Feels good—using pulley and wts. to increase power and decrease spasticity of arms. Spasticity of legs still marked.
Feb. 29.				<i>Lumbar puncture.</i> Saline lavage.
Mar. 5.				G. C. good—upper and lower extremities still stiff, but can move arms readily. Can not walk.
Mar. 11.				Legs improving. Can stand beside bed unassisted, less spastic in arms; slightly less spastic in legs.
Mar. 22.	Arsphenamine	0.3	intravenously.	
Apr. 3.	"	0.4	"	
Apr. 8.				<i>Lumbar puncture.</i> Saline lavage.
Apr. 13.	"	0.3	"	Moves fingers and wrists slightly. Shoulder motion limited on account of spasticity and contractures. Neck moves freely and powerfully. Some flexion of legs.
Apr. 19.				Flexion of legs improving—adductor spasm.
Apr. 24.	"	0.4	"	No more headaches.
May 2.				Voluntary turning of arms improving; still very spastic.
May 4.	Arsphenamine	0.25	intravenously.	
May 8.	"	0.2	"	
May 10.	"	0.2	"	Feels better. Walks about from object to object. Feels dizzy when he walks and there is nystagmus from side to side.
May 12.	"	0.2	"	
May 15.	"	0.2	"	Blood Wassermann two-plus.
May 21.				Decidedly improved by arsphenamine injections. Wassermann spinal fluid 0.1 to 1 c.c. four-plus, + + + +, Globulin one-plus, 8 cells per c.mm.

Transferred to Montefiore Home.

*Treatment at Montefiore Home*

1916

June 20.

July 4. Arsphenamine intravenously 0.16.

July 12. " " 0.4.

Aug. 9. " " 0.16.

Sept. 20. " " 0.3.

Oct. 4. " " 0.16.

Oct. 16. " " 0.16.

Nov. 4.

Nov. 25. Hg. inunct. 5 II, q.d. begun.

Nov. 27. Arsphenamine intravenously 0.3.

Dec. 6. " " 0.3.

Dec. 14. " " 0.3.

1917

Jan. 11. " " 0.3.

Jan. 23. " " 0.3.

Feb. 1. " " 0.4.

Mar. 12. " " 0.6.

Nov. 25, 1916, to Jan. 20, 1917. Hg. Inunct. 3 ii daily.

Nov. 25, 1916, to Mar. 10, 1917. KI gr. xv, t.i.d.

Considerable dexterity in upper extremities. Able to feed himself and button clothing. Some voluntary motion in lower extremities—partially inhibited by adductor spasm.

CASE 4

J. G., forty-five years old. A picture maker. Was infected with syphilis 30 years ago for which little treatment was received. For about 8 or 9 months he has been suffering from frequent basal headaches and his vision has been failing. For the past eight days his left arm has been feeling gradually heavier, and for the past five days his lower extremities have felt weak. He has also noted difficulty in grasping objects with his hands which are very weak. Admitted to the Hospital October 13, 1917.

*Physical Examination.*—Pupils irregular and react sluggishly to light. Both upper extremities weak, especially left and muscles of left hand are atrophied. Reflexes lively. Bilateral Babinski. Right greater than left. Sensation in arms diminished irregularly. Gait slightly spastic—very little ataxia evident.

*Lumbar puncture*—231 cells (lymphocytes) per c.mm. Globulin two-plus, Wassermann reaction 0.1-1 c.c. four-plus (+++++) positive.

Blood Wassermann, four-plus positive (+++++).

*Treatment* begun October 18, 1917.

1917

Oct. 18. Arsphenamine 0.25 intravenously.

Oct. 20. " 0.25 "

Oct. 25. " 0.3 " *Lumbar puncture*—44 cells c.mm.

Oct. 27. Arsphenamine 0.25 intravenously. Condition in arms unchanged. Feels better.			
Nov. 1.	"	0.25	"
Nov. 4.	"	0.25	"
Nov. 8.	"	0.3	"
Nov. 10.	"	0.3	"
Nov. 12.			
Nov. 15.	"	0.3	"
Nov. 17.	"	0.25	"

Power in left arm now returning.

Lumbar puncture—3 cells c.mm.

Marked improvement in general condition. No pains or aches. Power returning very rapidly.

Improvement remarkable and progressive. Patient able to return to work. Has been under moderately intensive treatment for a short while, followed by arsenobenzol and mercurial injections at stated intervals, about twice a month for arsenobenzol, with a course of mercurial injections every few months. Feels fine—is working. Both spinal fluid and blood are improved but there is a residuum of weakness and atrophy in left hand. Initial objective findings in reflexes unchanged. Spinal fluid now negative up to 0.6 c.e., cytology normal, Globulin negative.

*Diagnosis.*—Leptomeningitis cervicalis (luetica) with anterior horn or root involvement. Meningitic process cured. Note rapid diminution in biological factors under intravenous treatment and occasional lumbar puncture.

#### CASE 5

H. F., thirty-four years old, single, was admitted on January 27, 1917, with a history of infection with syphilis 7 years previously. For the past five months he has had occipital headaches and for the past three months his right leg has been "paralyzed." He has gradually lost control of his tongue and headache has grown more intense. There is shooting pain down the left leg. His left upper extremity is weak and he can move about only with great difficulty. For the past week diplopia has been present.

*Physical Examination.*—Patient is very emotional and very anxious. Has left upper lid ptosis, incomplete paralysis of right external rectus, with some weakness also in left external rectus. Pupils irregular, react sluggishly to light, and left is larger than right. There is slight nystagmus on looking to the right. Webber and Rinné positive. Right facial weakness and corneal anesthesia. Left grip weaker than right. Left K. J. greater than right. Left Achilles weaker than right. Incomplete left hemiplegia. Bilateral Kernig present.

Lumbar puncture—6 cells, c.mm. Globulin two-plus, Wassermann 0.1-1 c.e. four-plus. Blood Wassermann negative.

Treatment begun Jan. 29, 1917,	Neoarsphenamine	0.3
Feb. 1,	Arsphenamine	0.2
Feb. 3,	"	0.25

Evidence of extension of lesion to medulla. Breathing becoming irregular. Objective symptoms unchanged. Respiratory movements gradually more irregular and feeble and sudden exitus in spite of stimulation. One of a few cases where the lesion was rapidly fatal by medullary involvement by the syphilitic process. Involvement of the vital centers can be suspected in cases with sudden or gradual onset of respiratory and cardiac irregularity and embarrassment with or without a sharp rise in temperature.

## CASE 6

S. H., thirty years old, acquired lues some years previously and for it he was inadequately treated. About three months ago he developed a tumor of the testis which, after removal, was proved to be syphilitic. His blood was then found to be strongly positive with the Wassermann reaction.

On October 4, 1915, patient was admitted to the hospital with a history that for two months he had been suffering from severe headaches, frontal and parietal, and generalized pains in body more marked in right knee and shoulder. Four days before admission patient awoke from sleep and found he could not use right arm, his hand failed to grasp objects and he dragged his right leg on walking. There was some difficulty in urinary control, but no incontinence. On admission patient was slow in answering questions and complained of intense headache.

*Physical Examination.*—Eyes negative, except for right corneal anesthesia. Right face flattened. Right abdominal diminished. Right grip weak and power in right arm diminished. Tricep jerks present. K. J. on right side lively. Babinski positive, right inexhaustible clonus. Right limb spastic. Complete loss of pain, temperature and touch sense involving entire right side of body. Deep sense of pain unchanged (thalamic syndrome).

*Lumbar puncture*—Wassermann entirely negative (0.1-1 c.c.), 0 cells, globulin 0.

Blood Wassermann—four-plus positive.

Two days after first intravenous injection of 0.45 neoarsphenamine (October 8) headaches ceased and sensations commenced to return on right side. After two further injections (on October 13 and October 25) of neoarsphenamine 0.45 each the symptoms entirely disappeared, power returned and the patient was almost entirely well. The Babinski and clonus disappeared. Treatment was interrupted on account of the difficulty in obtaining the drug at the time. The patient received injections of mercury intramuscularly. The lesion was probably thrombotic involving the internal capsule and optic thalamus.

Repeated examinations of the spinal fluid have resulted in negative biological reactions. Treatment has been persisted in for over two years and the blood Wassermann is now also negative. Patient feels well though not quite as strong as before the lesion occurred. Is able to work as a day laborer.

1915

Nov. 1. Neoarsphenamine 0.5 intravenously.

Nov. 4. Lumbar puncture—fluid entirely negative.

Dec. 1. " 0.45 "

Dec. 15. " 0.45 "

1916

Mar. 24. Arsphenamine 0.4 intravenously. Feels somewhat weaker on right side — gradually becoming stronger.

Apr. 27. " 0.4 "

May 12. " 0.4 "

May 26. " 0.4 "

June 9. " 0.4 "

June 23. " 0.4 "

1917

Feb. 27. " 0.3 " Lumbar puncture. Fluid entirely normal. Blood Wassermann normal. Slight headache. Stronger.

From Feb., 1917, to June, 1918, under occasional treatment with arsphenamine about once a month with occasional course of mercurial injections. Condition practically cured. Biological reaction in fluid and blood normal.

## CASE 7

B. W., thirty years old, married, a policeman, was admitted to the hospital on April 18, 1916, with a history of a sore on the perineum 13 years previously. No history of antiluetic treatment. Present illness began 1-1/2 months ago when patient fell from bed to the floor and on awakening found his right side paralyzed. He could not talk for several days. His condition has gradually improved. Never had urinary or bladder disturbance. Has frequent headaches and constant pain in region of occipital protuberance. His memory is poor; he is quite emotional at times, and there is still evidence of the persistence of aphasia.

*Physical Examination.*—Well-built young man, mentally alert. Pupils small and react sluggishly to light and accommodation. Some weakness of right side of face. Reflexes of abdomen very active. Left upper extremity normal; right upper spastic and held almost rigid. Fingers and wrist can not be moved. Forearm and hand cold, skin pale. Right lower extremity somewhat spastic and less rigid. K. J. and Achilles very active. Patellar clonus. Left lower extremity normal. Gait typically hemiplegic. Fundi showed right retinal arteriosclerosis. Incomplete aphasia for naming objects. Perseveration. Marked alexia. Emotionally unstable. Cries easily, especially when questioned to determine degree of aphasia.

*Lumbar puncture.*—Spinal fluid Wassermann positive (+++++) four-plus, 3 cells, 0 globulin. Blood Wassermann positive four-plus.

*Treatment* begun April 20, 1916. Between this date and June 2, a period

of 43 days, he received fifteen intravenous injections of arsphenamine—totaling 4.5 grams, and he was lumbar punctured five times. There was very little improvement in the subjective symptoms while the spasticity was entirely unchanged.

The biological reactions were practically unchanged. Treatment was then instituted once every week and up to August, 1916, he received eight further arsphenamine injections intravenously (2.5 grams) and occasionally some mercury. By constant physiotherapeutic measures the right arm was somewhat improved. The aphasia also was slightly bettered. The patient was able to perform the duties of a watchman in the Police Department. The serologic reactions were practically unchanged one year after the onset of the trouble but have not been determined recently.

This illustrates a vessel lesion involving a physiologically important area with permanent destruction of function.

#### CASE 8

S. S., thirty-three years old, was admitted December 16, 1915, to the medical service in a disoriented, irrational condition. In fact his condition was practically moribund and little hope was held out for his recovery.

*Physical Examination.*—Irregular pupils, reacting sluggishly. Left facial weakness. Some exaggeration of left arm reflexes and of both knee and Achilles jerks. No ankle clonus, Babinski or Oppenheim. No palsies.

*Lumbar puncture.*—Spinal fluid Wassermann positive (++++) four-plus. 112 cells (lymphocytes) c.mm. Increased globulin.

Blood Wassermann positive four-plus.

Most of the time patient was stuporous with occasional periods of excitability which latter state gradually supervened. On December 22 difficulty in swallowing was noted.

*Treatment* was begun on December 27, although little hope of improvement was entertained. Between December 27 and January 15 patient received eight injections of arsenobenzol, totalling 2.3 grams and was punctured twice. There was a rapid and progressive improvement noted and on the latter date the patient was oriented, conscious all the time and occasionally was cheerful in attitude. The cells in the spinal fluid were reduced to 17 per c.mm.—otherwise there was no change in the reactions. Between Jan. 15 and Feb. 15, he received 12 injections of arsenobenzol (3.9 grams) and 2 grains of calomel by deep injections with further mental improvement and gradual reduction of cells in fluid to normal. The kidneys remained normal. Speech showed a characteristic parietic tremor which so far was uninfluenced by treatment. Between February 15 and March 9 patient received only two injections of arsphenamine (herpes of nose supervened) but was lumbar punctured twice with fluid being under considerable pressure. His condition, despite the previous almost moribund condition, improved rapidly and he was soon out of bed playing cards with other patients in the ward from whom he occasionally won. On March 9 he left the hospital with instructions to return later for further treatment. He was readmitted April 11 having gained 18 pounds in weight since leaving

the hospital. He complained of some headache and his wife stated that at night during sleep there was a "muttering delirium."

1916

<i>Apr. 11.</i>	Arsphenamine	0.4	intravenously.	
<i>Apr. 18.</i>	"	0.4	"	Gained seven pounds in last week. Mental condition was bright and alert though his speech betrayed distinct paretic characteristics.
<i>Apr. 27.</i>	"	0.3	"	Improvement continues.
<i>May 12.</i>	"	0.2	"	
<i>May 15.</i>	"	0.2	"	Wife thinks his condition less satisfactory mentally; he talks to himself occasionally and does not sleep well.
<i>May 19.</i>	"	0.3	"	Appetite good, sleeps better, and on the whole is in better condition than one week ago. Has had no reactions to the injections of arsphenamine and his kidneys are unaffected by the intensive treatment.

On June 9 patient returned for treatment in poor condition and his wife stated his mental condition was unsatisfactory as patient talked to himself a good part of the time.

On physical examination there was no objective change but patient was extremely nervous and irritable, muttering to himself. Since March 9, a period of three months, he has received only five injections of arsphenamine, totaling 1.4 grams.

*June 9, 1916.*—Arsphenamine 0.3 intravenously—part of a solution administered to other patients in the ward with no ill effect. Four hours later he became gradually unconscious. Twitching of hand began and finally a violent clonic convulsion which involved the entire left side of body, being controlled by the administration of chloroform. One hour later a second convulsion involved the entire body. Breathing was stertorous and patient remained unconscious. Lumbar puncture revealed fluid under high tension but was not followed by relief of the symptoms.

Between June 9 and 13, patient remained stuporous most of the time with occasional twitchings in the hands and occasional attacks of respiratory difficulty and cyanosis of bulbar origin. Urination was involuntary, but there was apparently considerable diminution in the total amount finally leading to complete suppression before death.

Four days after the onset of the symptoms the patient became gradually worse and died.

This patient practically moribund on admission was gradually improved to the point where he was able to take care of himself. He played cards and was able to go about alone; with the gradual diminution of intensive treatment, the



patient gradually relapsed and succumbed to what appeared to be a profound intoxication.

## CASE 9

B. A., thirty-eight years old, married, a very intellectual, professional man. One healthy child three years old. Acquired lues about ten years ago, the initial lesion being located on the tonsil. Diagnosis was confirmed by the appearance of a secondary roseola and a positive Wassermann reaction in the blood.

From the very onset of the secondary symptoms until January, 1917, a period of almost nine years, patient received persistent and vigorous mercurial treatment by injections together with about six injections of neoarsphenamine intravenously in 1916. The treatment was badly borne and the blood reaction was unchanged. Patient came under our observation in January, 1917.

Physical examination showed absolutely no objective signs of constitutional or nervous lues and no intellectual deterioration. Lumbar puncture advised as routine but refused. Blood Wassermann four-plus (++++).

Between January, 1917, and November, 1917, patient received 18 injections of arsphenamine of 0.4 grams and 12 injections of Hg salicylate and a course of 30 inunctions without a reaction and with apparent benefit to his general condition.

Lumbar puncture in November, 1917, revealed a Wassermann reaction positive (++++) four-plus 0.1-1 c.c., 50 cells to the c.mm. and increased one-plus globulin. Gold solution showed syphilitic curve. Blood Wassermann four-plus.

No objective or subjective signs of nervous involvement. Patient's wife was warned to report first signs of change in patient's mental condition, habits or character.

Between November, 1917, and May, 1918, patient received six additional intravenous injections of arsphenamine and 14 injections of mercury salicylate intramuscularly.

During May, 1918, patient's wife reported the first signs of mental change. Patient became indifferent to his surroundings, sitting in company with apparently little interest in conversations, became somewhat depressed and pessimistic, telling his wife his life had been a failure, found himself unable to keep up his work of managing building construction and lost his way home on two occasions.

*Physical Examination.*—Marked depression. Slight facial tremor and tremor of hands. No other objective change. Speech somewhat, though very slightly, impaired with occasional stumbling over phrases. Barely perceptible intellectual deterioration; somewhat indifferent to surroundings.

Blood Wassermann four-plus (++++). Spinal fluid unobtainable.

*Diagnosis.*—General paresis. This patient was under vigorous mercurial treatment by injection and inunctions from the very onset of the disease. The reaction persisted in the blood in spite of additional arsphenamine injections. The findings of a positive spinal fluid Wassermann (no paretic curve) together

with the persistence of the positive blood reaction suggested the eventual development of a paresis as a possibility. This unfortunately has occurred.

## CASE 10

A. F., thirty-five years old, married, transferred from the medical service to which he was admitted for marked jaundice of one month's duration, weakness of left arm and leg for ten months, constant, severe headache for eleven months, emaciation, general weakness and mental apathy. Occasional attack of lightning pains down both legs. Ten months ago had left-sided paralysis of sudden onset.

*Physical Examination.*—Emaciation, General adenopathy. Marked generalized jaundice. Weakness left arm and leg. Irregular sluggish pupils, ptosis of right lid (incomplete), sluggish reaction of pupils to accommodation. Liver distinctly palpable. Knee and Achilles jerks present. No Babinski or clonus. Normal bladder control. Mentality sluggish, patient constantly complaining of headaches. Speech not affected nor suggestive of dementia paralytica.

Blood Wassermann strongly positive (++++) four-plus.

Spinal fluid Wassermann strongly positive 0.1-1 c.e., (++++ 4 lymphocytes to the c.mm. Globulin positive.

*Diagnosis.*—Cerebrospinal lues. Syphilis of the liver.

Treatment began August 15, 1916. Urine negative. Jaundice less marked.

1916

Aug. 15. Arsphenamine 0.3 intravenously.

Aug. 17.       “       0.3       “

Aug. 19.       “       0.3       “

Sept. 1.       “       0.3       “

Jaundice rapidly disappearing. Headache less intense. Patient is rapidly improving. Discharged Sept. 4, 1916, with instructions to return in one week for further treatment.

Nov 9. Arsphenamine 0.4 intravenously. Somewhat improved. Jaundice gone.

Still has some headaches and occasional attacks of pain in legs.

1917

Jan. 6.       “       0.3       “       Still has headache and pains in legs.

Spinal fluid and blood still reveal strongly positive Wassermann reactions. Patient improved mentally but still dull.

Jan. 16 to Apr. 15, 1917, patient received six injections of arsphenamine 0.35 gram intravenously. Headaches and other pains disappeared and he became bright and active mentally. The somatic signs were unchanged as were the biological reactions. Patient resumed work and from time to time came to the clinic for observation and mercurial injections. There was not definite evidence on which to base a diagnosis of general paresis.

One year later patient returned to the hospital with a typical paretic speech

and with definite signs of intellectual deterioration, so that a diagnosis of general paresis was unquestionable.

Blood and spinal fluid were positive four-plus (++++) . Gold solution reaction was typical of general paresis.

## CASE 11

R. G., thirty-nine years old, married, a waiter, contracted a chancre twenty years ago. Was referred to the hospital for treatment on February 24, 1917, with a diagnosis of tabes dorsalis, his chief complaint being lancinating pains in both lower extremities on and off for six years. He found it difficult to pursue his duties as a waiter on account of the pains and weakness in his legs. Occasionally his urine is voided involuntarily and for some years he has been impotent. He has noted a tremulousness in his speech for some months and his memory is not quite as good as it used to be.

*Physical Examination.*—Fixed pupils which react to accommodation. Knee and Achilles jerks absent. Romberg positive. Diminished hearing left ear. Moderate hypotonia. Tongue and lips show suspicious tremor. Speech somewhat hesitant, but not characteristic of dementia paralytica. Absolutely no evidence of intellectual deterioration although the possibility of an early paresis is kept in mind.

Blood Wassermann positive (++++) four-plus.

Spinal fluid Wassermann positive 0.1-1 c.c. four-plus (++++) , 1080 cells c.mm. Globulin plus (+).

As the patient could remain in the hospital only one day, he received on February 24, 1917, 0.4 gram arsphenamine and his spinal fluid was withdrawn. Two weeks later he again received 0.3 gram arsphenamine and 30 c.c. of spinal fluid was withdrawn. Examination of this fluid after one intravenous injection and one tapping showed a reduction in the cell count from 1080 cells on February 24 to 141 cells per cubic millimeter. Two weeks later a similar treatment was given with a further reduction of the cell count to 120 cells. The Wassermann test of the fluid was now only two-plus in 0.6 c.c., being negative up to 0.5 c.c. and completely inhibited (four-plus) in 0.8 to 1 c.c.

The clinical improvement was decidedly marked. The pains were much lighter and he was able to control his urine completely.

Three further intravenous injections were given on April 7, 21 and May 5 (0.3 gram each) and on May 19, intraspinal injections following withdrawal of 30 to 40 c.c. of spinal fluid were begun.

1917

May 19.	Arsphenamine	0.3	intravenously.	15	c.c.	normal	serum	intraspinally
						(inactivated).		
June 2.	"	0.3	"	15	c.c.	normal	serum	intraspinally
						(inactivated).		
June 30.	"	0.3	"	15	c.c.	normal	serum	intraspinally
						(inactivated).		
July 21.	"	0.3	"					
Sept. 5.	"	0.3	"					

Oct. 6.	Arsphenamine	0.3	intravenously.	
Oct. 20.	"	0.3	"	Blood Wassermann (±).
Nov. 3.	"	0.3	"	Lumbar puncture { 0.4 negative, Wassermann { 0.6 +++ { 0.8-1 c.c. ++++
Nov. 24.	"	0.3	"	15 c.c. normal serum intraspinally.
Dec. 8.	"	0.3	"	15 c.c. normal serum intraspinally.
Dec. 22.	"	0.3	"	
Dec. 29.	"	0.3	"	Lumbar puncture—53 cells c.mm.
1918				
Jan. 12.	"	0.3	"	Lumbar puncture—30 cells c.mm. Wassermann { 0.4 negative spinal fluid { 0.6-1.0 c.c. { ++++
Jan. 26.	"	0.3	"	
Feb. 9.	"	0.35	"	Lumbar puncture—27 cells—0.4-1 c.c. ++++. Globulin negative.
Mar. 2.	"	0.3	"	
Mar. 16.	"	0.4	"	
Apr. 12.	"	0.4	"	
Apr. 27.	"	0.4	"	

The patient's condition is improved. He has very little, if any, pain. His gait is quite normal and he can work as a waiter. So far he has not deteriorated intellectually and a diagnosis of general paresis is not warranted. The clinical and biological improvement were more marked during intravenous therapy alone, hence this treatment has been resumed with satisfactory results.

#### CASE 12

S. F., came for treatment January 24, 1916. The initial lesion occurred about ten years previously for which he had been under intermittent treatment for four or five years. For the past year his eyesight had become progressively worse and he had suffered with increasingly severe fits of mental depression necessitating long vacations and absence from business. For the past month he has been markedly depressed, unable to concentrate his attention upon his business and shunned the society of his friends. His memory was good for recent and past events but he volunteered no information, refusing to talk. There were no delusions or hallucinations and no ideas of grandeur. His eyesight was gradually failing so that he could only read the large headlines of a newspaper with difficulty. There was gradual diminution in sexual desire and difficulty in starting the urinary stream.

*Physical Examination.*—Pupils fixed and irregular. Primary optic atrophy of the left eye almost complete. Right eye shows a marked neuroretinitis. The knee and Achilles jerks are absent. Slight ataxia. No Romberg. No speech defect.

Blood Wassermann +++.

Spinal fluid Wassermann positive four-plus (++++) 0.1-1 c.c., 60 cells per c.mm., and globulin ++.

He received three arsphenamine injections intravenously and four lumbar punctures were done, 30 c.c. of fluid being removed and replaced by 15 c.c. of his own serum inactivated and nonmedicated.

After the third puncture the Wassermann was positive from 0.6 to 1.0 c.c. +++++; 20 cells per c.mm. + globulin, and after the 4th puncture three months after the beginning of the treatment, the spinal fluid was entirely negative 0.1 to 1. c.c.; 3 cells to the c.mm., and there was only a faint trace of globulin. The blood was negative.

Symptomatically the patient was "cured." He felt like a new man and was again able to take care of his immense business interests. The left eye showed no improvement. The right eye gradually improved so that he was able to read a newspaper with ease. The report of the ophthalmologist showed 20/30 vision in this eye.

During the remainder of 1916 he received seven injections of arsphenamine (0.4) and during 1917 he received two injections of arsphenamine and numerous injections of mercury salicylate intramuscularly. Intravenous treatment was not pushed, contrary to our recommendation, because of the patient's and ophthalmologist's fear of injury to the optic nerve.

In April, 1918, vision again became progressively impaired and the right eye now showed progressive contraction of the field of vision.

Spinal fluid positive 0.1-1 c.c. +++++, the cells are increased (55 c.mm.), and the globulin is ++. Blood Wassermann negative.

Illustrating the influence of treatment with nonmedicated serum intraspinally on the Wassermann reaction of spinal fluid with apparent arrest of disease. Relapse after two years with progression of lesion, possibly due to insufficient treatment. Clinically the relapse involves only the optic nerve, the remainder of the tabetic condition being *in status quo* and satisfactory.

#### CASE 13

M. Z., fifty years old, tailor, acquired lues 30 years ago. Admitted to the hospital in August, 1916, complaining of weakness and pains in legs, inability to walk and double vision. For the past two years has difficulty in starting urinary stream.

*Physical Examination.*—Argyll Robertson pupils. Left internal strabismus. Ptosis of left lid. Knee and Achilles jerks absent. Gait very ataxic, walking alone impossible. Brought to hospital in ambulance. Romberg very marked.

Blood (+++) positive Wassermann.

Spinal fluid Wassermann 0.1-1 c.c. positive (++++). 16 cells c.mm. Globulin +.

	1916	gram
Aug. 4.	Arsphenamine	0.3 intravenously.
Aug. 11.	"	0.35 "
Sept. 9.	"	0.3 "

Improved. Stronger. Walks a little. Less pain. Diplopia and ptosis less marked. Following injection severe reaction. Chill. Temperature 104° F.

1917

<i>Jan. 15.</i>	Arsphenamine	0.3	intravenously.	No treatment since above, condition same as on admission. Pains in legs and inability to walk.
<i>Jan. 25.</i>	"	0.3	"	Lumbar puncture: spinal fluid Wassermann 0.1-1 c.c. positive + + + +, 7 cells c.mm. Globulin +. Blood Wassermann + + + + positive.
<i>Feb. 8.</i>	"	0.3	"	Markedly ataxic—can't walk much.
	15 c.c. salvarsanized serum intraspinaly (0.00025 gram ar-sphenamine).			
<i>Feb. 27.</i>	Arsphenamine	0.3	intravenously,	No better—can't walk much.
	15 c.c. salvarsanized serum intraspinaly (0.0005 gram ar-sphenamine).			
<i>Mar. 13.</i>	Arsphenamine	0.3	intravenously,	Gait worse after intraspinal treatment.
	15 c.c. salvarsanized serum intraspinaly (0.00075 gram ar-sphenamine.)			
<i>Mar. 27.</i>	Arsphenamine	0.4	intravenously,	
	15 c.c. salvarsanized serum intraspinaly (0.00075 gram ar-sphenamine).			
<i>Apr. 7.</i>	Arsphenamine	0.4	intravenously,	
	15 c.c. salvarsanized serum intraspinaly.			
<i>May 15.</i>	Arsphenamine	0.3	intravenously,	
<i>June 12.</i>	"	0.3	"	No better as to gait in spite of 12 intravenous and 5 intraspinal injections.
<i>June 28.</i>	"	0.3	"	
<i>July 19.</i>	"	0.3	"	Reeducational treatment begun. Spinal fluid 8 cells, globulin +, Wassermann reaction 0.1-1 c.c. + + + +.

Intravenous injections of arsphenamine about every three or four weeks from September to June, 1918. Pain abolished. Stronger. After a number of re-educational treatments, gait steadily improved so that patient can now walk with a cane whereas when intraspinal treatment was suspended patient had to be brought to hospital in a wheel chair.

Intravenous treatment administered every 2 to 4 weeks with occasional course Hg and KI during past year. Can now walk unassisted with help of a cane, is stronger, feels better and can control urination. Improvement dates from the beginning of reeducation according to Maloney method.

CASE 14

L. D., twenty-three years old, single, a typist, admitted on November 3, 1912, with a history of normal development and good health until fifteen years of age when she lost considerable weight and began to have severe headaches. Her present illness is of six months duration. She has convulsive seizures of the Jacksonian type beginning in right hand and spreading to the arm and leg, followed by unconsciousness. These attacks are occasionally preceded by severe headache and pain over the left eye and by vomiting. For the past few months her eyesight has been failing and for the past few weeks she has difficulty in speaking.

*Physical Examination.*—Appears dull and apathetic. Right arm and right leg paretic; reflexes on right side livelier than on left. Slight right exhaustible ankle clonus. No Babinski, no Oppenheim. Bilateral choked discs, 1-2 diopeters.

Wassermann negative in blood and spinal fluid. Record of cells and globulin not obtainable.

On November 22, 1912, patient had an attack in the ward, affecting right arm and leg which were convulsed for  $\frac{1}{2}$  hour. Attack began in right arm. No loss of consciousness.

*November 29, 1912.* Exploratory craniotomy in left temporal region. Fine pearly white exudate in pia. No tumor found. Swelling of discs disappeared after operation. Patient was discharged on January 3, 1913, with slight headache and a diagnosis of cerebral neoplasm.

Patient readmitted on April 3, 1913, complaining of incessant headache. Three weeks ago vomited incessantly for one week. She has tingling and numbness in her hands and feet and girdle across lower abdomen. Eyesight again becoming bad. Very slight edema of discs on ophthalmoscopic examination.

*Spinal fluid:* negative Wassermann 0.1-1 c.c., 40 cells (lymphocytes) per c.mm. Lues cerebri suspected and arsphenamine given intravenously.

1913

*June 11.* Arsphenamine 0.3 intravenously. Right leg rigid from hip down and feels cold and dead. Occasional tingling.

*July 27.*       “       0.3       “       Convulsive seizures right arm and leg. Pupils dilated. Slight papilledema discs.

*Lumbar puncture*—Fluid under increased tension. 25 cells per c.mm. Wassermann weakly positive in 1 c.c. Blood negative.

*Nov. 11.*       “       0.3       “       Has had severe headaches for two weeks. Very slight blurring of discs and eyes hypermetropic.

Nov. 17.				<i>Lumbar puncture</i> —pressure 350 mm. Wassermann positive in 1 c.c., negative 0.1, 41 cells c.mm., globulin $\pm$ .
Nov. 17.	Arsphenamine	0.3	intravenously.	
Dec. 8.	"	0.3	"	<i>Lumbar puncture</i> —spinal fluid Wassermann negative 1 c.c.—10 cells.
Dec. 24.	"	0.3	"	<i>Lumbar puncture</i> —spinal fluid Wassermann negative 1 c.c.—4 cells.
1914				
Mar. 2.	"	0.3	"	Blood now positive + + + +, <i>spinal fluid</i> 19 cells, also positive (+ + + +) in 1 c.c. Gradual improvement in all symptoms under arsphenamine therapy.
June 15.	"	0.3	"	Fluid now only 140 mm. pressure. Wassermann on blood and spinal fluid are again negative, 27 cells in c.mm., and globulin +.
1915				
Jan. 7.				<i>Lumbar puncture</i> —greatly improved under arsphenamine therapy. Fundi now normal. Spinal fluid and blood negative. 19 cells, globulin + +.
Jan. 8.	Arsphenamine	0.3	intravenously.	This injection was followed by faintness, vertigo, spasm left upper extremity, thumbs turned into palm, fingers hyperextended, pupils dilated and did not react to light. Hearing impaired in right ear. On the 9th, patient was better, though there was some difficulty in sensory localization.
Jan. 21.				<i>Lumbar puncture</i> —Headaches persist and there is pain over left upper abdomen. Fundi show chorioretinitis with minute patches indicative of hereditary lues. Father's blood proved to be positive + + + +. Spinal fluid negative 0.1-1 c.c. 231 cells per c.mm. Globulin + +.

Patient was readmitted on March 11, 1915, on account of severe headaches. *Lumbar puncture* again revealed clear fluid under great pressure, with a negative Wassermann test and 25 cells to the c.mm., globulin + +. Puncture relieved the headache. Fundi normal. Pupils react to light and accommodation. No palsies. Extremities negative. No sensory changes. No ataxia. Possible Babinski in left side. Only sign found is difficulty in reproducing difficult positions of fingers. Blood Wassermann negative.



1915

- Mar. 12. Arsphenamine 0.3 intravenously. No reaction.
- Apr. 26. " 0.3 " Intense headaches and nausea, vomiting and tinnitus for ten days before admission. *Lumbar puncture*—spinal fluid under great pressure again.
- Apr. 27. Patient discharged relieved of headache.
- May 6. *Lumbar puncture*—readmitted on account of headache which is throbbing and almost constant and frontal. Frequent vomiting. Hearing becoming worse.
- May 7. Arsphenamine 0.3 intravenously. On following day, patient restless and irritable all day. Looks about room and under sheets uttering the words "I'm afraid." Constantly rubs left hand over mouth and pulls at hair.
- May 9. Was turbulent all night and became entirely unmanageable. Hallucination of hearing. Received hyoscine and *lumbar puncture* performed, but the maniacal condition was not affected.
- May 10. Quieter. Fabricates events of previous day. Still talks in rambling manner. Discs normal. Gradual improvement. Put on iodide of sodium medication.
- May 22. Headache gone. Pupils irregular—right pupil greater than left.
- June 2. *Lumbar puncture*—10 c.c. removed. Fluid negative Wassermann 1 c.c. Globulin ++, 9 cells.
- June 9. *Lumbar puncture*—20 c.c. removed. Right pupil greater than left. Headache gone. Patient discharged and later sent to King's Park Asylum by her folks for maniacal condition similar to above. Case diagnosed at this institution as dementia paralytica.

Dec. 30.

*Lumbar puncture*—Readmitted on account of frontal headache and pain over left upper abdomen. Mentally normal. Fundi again show patches of chorioretinitis.

1916

Jan. 5. Arsphenamine 0.2 intravenously. Blood Wassermann negative. No change in physical signs. Fine facial and lingual tremor. Receiving injections of calomel.

Jan. 17. Arsphenamine 0.2 intravenously.

Jan. 19. " 0.2 "

Jan. 24. " 0.3 "

Jan. 31. " 0.2 "

Condition now very satisfactory. To return for further treatment.

Feb. 7. " 0.3 "

Feb. 18. " 0.2 "

Aug. 23. " 0.3 "

Gets occasional headache and some dizziness. Occasional temporary loss of speech. Is able to work.

Aug. 23.

*Lumbar puncture*—spinal fluid—3 cells, globulin 0, Wassermann negative. Blood Wassermann negative.

1917

Aug. 23. Arsphenamine 0.3 intravenously. Able to work. Occasional headache.

1918

Feb. 26.

Has been at work as a typist for the Government since September, 1917, and quite well until two weeks ago. Numb feeling in right leg to middle of thigh. Legs get heavy and stiff and she has to stop walking for five minutes. This has happened three times. No headaches or vomiting now. Pupils are slightly irregular but react. Hears whispered voice at five feet in previously defective ear. General condition now excellent. Left Babinski, right Babinski at times only.

Apr. 3. Arsphenamine 0.4 intravenously.

Apr. 20. " 0.35 "

Apr. 27. " 0.3 "

May 4. " 0.3 "

Practically normal. Feels fine. Able to work.

*Lumbar puncture*—blood and spinal fluid negative, 0 cells, 0 globulin.

This is a case of cerebral lues on a congenital luetic basis. The difficulty of diagnosis was marked. The first inkling as to the luetic nature of the lesion was the increased cell count. The positive Wassermann was late and evanescent. The early symptoms were those of cerebral neoplasm. Treatment was infrequent and interrupted due to severe reactions from intravenous injections of even small doses. Intraspinous medications (2) were followed by extremely severe reactions and had to be abandoned. In spite of these difficulties persistent treatment over a number of years (arsphenamine and mercury and iodide combined) has resulted in a cure.

## CASE 15

B. T., forty-six years old, married. Denies luetic infection. Was admitted for treatment on May 23, 1916, on account of nervousness. This has been getting worse for the past seven months. He has occasional severe headaches. For past five months his speech has been affected. He has become impotent. His wife has tabes dorsalis. One daughter has a four-plus Wassermann. Family report that he is easily excited, irritable and shows marked deterioration in intellect.

*Physical Examination.*—Well nourished. Mentally confused. Memory poor, emotionally unstable. Very irritable at times. Speech typically parietic. Tremor of tongue and face. Right pupil does not react. Left pupil reacts sluggishly. Reflexes present elsewhere.

*Lumbar puncture*—spinal fluid Wassermann ++++ 0.1-1 c.c. positive. Parietic curve (gold solution). 12 cells c.mm. Globulin ++.

1916

May 24. Arsphenamine 0.2 intravenously.

May 26. " 0.3 "

May 29. " 0.35 "

May 31. " 0.3 "

June 2. " 0.4 "

June 5. " 0.4 "

June 7. " 0.35 "

June 13. " 0.4 "

*Lumbar puncture.*—Saline lavage (20 c.c.). Considerably improved. Less nervous—less irritable. Still can not control emotions entirely. Speech unaffected.

June 26. Arsphenamine 0.4 intravenously.

July 3. " 0.3 "

July 10. " 0.4 "

Progressive improvement. Emotionally unstable at times.

For the remainder of the year 1916, patient received 12 injections of arsphenamine intravenously (4.4 grams) and was occasionally lumbar punctured. There was gradual and progressive improvement in his condition. In fact he became quite well mentally. His memory and judgment were normal. His emotions were controlled. The blood and spinal fluid Wassermann tests remained positive +++. The cells and globulin in the fluid became normal. During the first

half of 1917 the patient received two intravenous treatments a month—every other treatment being accompanied by an injection of 15 c.c. normal inactivated auto serum intraspinally after removal of 20-30 c.c. of spinal fluid. The biological reaction in the fluid was thereby reduced to 0.2 ++ 0.4-1 c.c. ++++. The blood was unchanged. This treatment was persisted in once a month during the remainder of 1917 and the first half of 1918. The patient has been steadily at work. His mentality is practically normal. He presents no objective signs with the exception of a slight hesitancy in his speech and a very fine facial tremor. His folks regard him as normal. The remission has persisted up to date after two months' freedom from treatment.

## CASE 16

G. B., forty-two years old, married. Denied an infection with lues. Was admitted to the hospital on April 4, 1916, on account of nervousness. Two years previously he had an "attack" lasting about two hours during which time he could not speak. Patient is a foreigner and has been in this country a short time and can not speak English. He has had a university education, and was an attorney in his native Hungary. Since here has made a precarious living by selling stockings but recently has so deteriorated that he had to give up this work. A few weeks ago he had a repetition of his aphasia attack of two years ago. No loss of consciousness. In spite of his change in social position he is apparently well satisfied with his present surroundings. He is unstable emotionally, his speech is thick and hesitant, he stumbles in test phrases and his mentality is decidedly deteriorated.

*Physical Examination.*—Pupils and ocular muscles show no abnormality. Reflexes hyperactive. Some tremor of face and tongue. A typical general paretic.

Blood Wassermann positive ++++.

Spinal fluid Wassermann 0.1-1 c.c. positive ++++. Paretic curve (gold solution). Cells 20, globulin +.

1916

Apr. 6. Arsphenamine 0.3 intravenously.

Apr. 7. " 0.3 "

Apr. 10. " 0.3 " Says he feels better and is less nervous. Objectively no change. Asks to be discharged to return for treatment in 1 week.

Apr. 15. " 0.3 " Generalized macular rash which disappeared in a few weeks.

May 17. " 0.3 "

May 24. " 0.3 "

May 31. " 0.3 "

June 7. " 0.3 "

July 24. " 0.3 " Feels much better. Able to go to work. Speech better, sleeps well, less nervous.

This patient on account of the necessity of earning a living could not return for further treatment. He has been at work steadily for over a year in a munition plant. His condition is stationary. There has been no marked evidence of progression of the lesions. The objective signs are practically unchanged.

## CASE 17

W. I., forty years old, married, was infected ten years previously by contact with a member of the family who subsequently died of general paresis. For the past four or five years he has been under intermittent treatment by injections and inunctions of mercury and potassium iodide internally.

Two years ago blood Wassermann was reported negative. Five months ago he began to be argumentative and irritable and finally became obstreperous.

Blood and spinal fluid were found to be positive, and his physician began intravenous injections of salvarsan and salvarsanized serum intraspinally. After two treatments patient became worse, finally being removed to a private asylum for the insane in an irrational and maniacal condition. While at this institution he received about ten injections of salvarsanized serum intraspinally and intravenous injections of arsphenamine, with some improvement.

One month before admission, on April 10, 1916, patient insisted on leaving the asylum. On discharge, patient was very euphoric and expansive. Had visual and auditory hallucinations and was typically parietic in speech.

Treatment was begun on April 10, 1916, and was instituted as follows:

1916

*Apr. 10.* Neoarsphenamine 0.75 intravenously, Lumbar puncture. Spinal fluid—positive 0.1-1 c.c. ++++. Blood positive +++, cells 10, globulin +. Paretic curve (gold solution).

*Apr. 17.* “ 0.7 “

*Apr. 24.* “ 0.9 “

*May. 1.* Arsphenamine 0.4

*May. 5.* “ 0.4 Lumbar puncture.

*May. 8.* Arsphenamine 0.4 intravenously,

*May. 12.* “ 0.4 “

*May. 17.* “ 0.4 “

*May 27.* “ 0.4 “

*June 1.* “ 0.5 “

*June 5.* Lumbar puncture. Spinal fluid 0.4-1 c.c. positive +++, cells 0, globulin +, colloidal Gold: Paretic curve.

*June 12.* Arsphenamine 0.4 intravenously,

*June 19.* “ 0.4 “

*June 26.* “ 0.4 “

*June 30.* “ 0.4 “

*July 5.* “ 0.4 “ Blood Wassermann now negative.

During July and August injections of 0.06—0.12 Hg salicylate every five days.

*Aug. 28.* Lumbar puncture. Spinal fluid negative up to 0.8, 1 c.c. ++, 0 cells, ± globulin.

About this time a decided remission in symptoms set in and patient was able to return to his work as a salesman. He did very good work. His mental condition was decidedly improved, although on occasions his ideas were expansive and he was somewhat euphoric. His speech was slightly hesitant. There were no gross signs of intellectual defect.

1916

*Sept. 9.*

*Lumbar puncture*—30 c.c. removed—  
Wassermann negative, 0 cells, globulin 0.

*Sept. 23.* Arsphenamine 0.4 intravenously.

*Sept. 30.*

*Lumbar puncture*—30 c.c. removed—  
Wassermann 0.1-1 c.c. negative,  
0 cells, globulin 0.

*Oct. 3.*

Condition decidedly improved. Practically well.

*Oct. 28.* Arsphenamine 0.4 intravenously.

*Oct. 20.* “ 0.4 “

*Nov. 1.* “ 0.4 “

*Dec. 11.*

*Lumbar puncture*—Wassermann 0.2—  
1 c.c. positive + + + +, blood + + + +.  
Biological reactions again positive.  
Somewhat more euphoric. Still at  
work and making a good record of  
sales. Speech somewhat thick.

*Dec 19.* Arsphenamine 0.4 intravenously.

*Dec. 29.*

Intraspinal injection normal serum  
15 c.c. (inactivated auto serum).

1917

*Jan. 8.* Arsphenamine 0.4 intravenously,

*Jan. 30.*

Intraspinal injection of 30 c.c. normal  
auto serum inactivated.

*Jan., Feb., and Mar., 1917,* Mercury salicylate gr. 1-2 every five days.

*Mar. 30.* Arsphenamine 0.3 intravenously.

*May 25.* “ 0.4 “

*May 29.* “ 0.4 “

*June 8.* “ 0.4 “

*June 16.* “ 0.4 “

Intraspinal injection of normal serum.

Commencing in June, 1917, there was a decided relapse of all the mental symptoms. Patient became argumentative, euphoric and expansive, had great schemes for business success showing poor judgment and insight. He was removed to a private hospital for the insane on account of inability to control his actions. Intravenous treatment every other week. Patient improved some-

what and became quiet and socially possible so that he was able to mingle with other patients. He remained in this condition for nearly another year.

Recently patient is gradually becoming weaker, his memory is feeble. He did not recognize his wife when she last visited him. He is elated and euphoric at times, though never violent or noisy. He has had no treatment for about 8 months.

## CASE 18

A. R., thirty-two years old, married. No history of syphilis. Was admitted to the hospital on April 11, 1916, with a history of intellectual deterioration for about two years. His character and ability have markedly deteriorated. He has drunk liquor to excess, gambled and lost about \$15,000 through bad investments. He is quite irritable and easily provoked, is boastful and very emotional. Is very suspicious of his friends and relatives. Sleeps poorly and gets up at all hours at night. During day he tires easily and gets into bed at any hour. Recently at another institution he received five intraspinal injections of salvarsanized serum.

*Physical Examination.*—Typically paretic. Very unstable emotionally. Laughs and cries easily. Forgetful. Memory good at times, but answers are retarded. Delusions of persecution. Left pupil greater than right; both react sluggishly to light and accommodation. Knee and Achilles jerks present. No Romberg, no ataxia. Blood positive +++++. Spinal fluid 0.1-1 c.c. positive +++++, 20 cells c.mm., globulin ++. Paretic curve (gold solution).

Treated intensively intravenously from April 14, 1916, until May 31, 1916. Received 17 injections of arsphenamine, a total of 6.2 grams in 49 days. There was no appreciable change in the patient's mental state apparent.

The treatment was continued with lumbar puncture about every second and fourth week, and arsphenamine injections as follows:

1916			
June 9.	Arsphenamine	0.3	intravenously.
June 19.	"	0.3	"
Sept. 6.	"	0.4	"
Sept. 19.	"	0.4	"
Sept. 27.	"	0.3	"
Oct. 14.	"	0.3	"
Nov. 6.	"	0.4	"
Nov. 28.	"	0.4	"
Dec. 12.	"	0.3	"
Dec. 19.	"	0.3	"
Dec. 26.	"	0.3	"

There was no appreciable change, patient was able to work as a waiter at times but his speech was typically paretic and he was very garrulous. Lumbar puncture revealed a positive +++++ Wassermann in 0.4-1 c.c., 8 cells c.mm. and globulin +. Blood Wassermann +++ positive.

The treatment was continued during 1917, about twice a month. Intraspinal injections were refused on account of the severe reactions of the first five treatments. The clinical condition was practically unchanged, though the pa-

tient kept at work and his family reported him as markedly improved in September, 1917. In the latter part of 1917, the patient slowly deteriorated and was removed to a state institution for the insane.

## CASE 19

J. F., thirty years old, single, telephone operator. Infected with syphilis six years ago. Admitted to hospital on September 7, 1916, on account of extreme nervousness, sleeplessness, and difficulty in enunciation of polysyllabic words. For past four months patient has been easily worried and is irritable and at times was thought irrational by friends.

*Physical Examination.*—Pupils irregular, rigid, do not react. Bilateral internal and external nystagmus. Cranial nerves negative. Knee and Achilles jerks present. No Romberg. No ataxia. Patient depressed about his inability to continue his work. Typical parietic speech. Emotional—agreeable and quiet most of time.

*Lumbar puncture*—spinal fluid Wassermann 0.1-1 c.c. positive + + + +, cells 28 c.mm. globulin +. Parietic curve (gold solution).

Blood positive + + + +.

Received intensive treatment intravenously commencing September 8, 1916. Arsphenamine 0.2 every other day until October 2, 1916, when he left hospital improved (less nervous and speech somewhat improved) to return once a week for additional treatment. On November 3, patient became excited and obstreperous and was removed to Manhattan State Hospital. On September 8, 1917, patient was still alive at this institution, and up and about with little change in his general condition. Recently he had a slight stroke lasting a few hours, with no residual paralysis. Mentally usually quiet and agreeable though at times quite expansive.

Wassermann spinal fluid reported + + + positive, 16 cells, globulin +. Blood negative.

Treatment at the asylum was purely symptomatic.

## CASE 20

S. S., fifty-one years old, married, admitted May 15, 1915. History of chancre 27 years ago for which he took internal medication for one year.

*Present Illness.*—Six months duration. Weakness lower limbs. General weakness. Impairment sexual power, vision, hearing and smell. Gait is becoming unsteady for past two months. Delay in urination for past five years.

*Physical Examination.*—Pupils pinpoint, immobile to light and accommodation. Deep reflexes active—K. J. and Achilles exaggerated. Gait slightly unsteady—somewhat spastic—Romberg positive.

Spinal Fluid—0.1-0.5 c.c. negative; 0.5-1.0 c.c. + + + +; 15 cells c.mm. Globulin + +. Blood Wassermann + (weak).

	1915		gm.
May 29.	Intrasp. inj. salvarsanized serum	0.00025	
June 12.	" " " "	0.0005	
July 8.	" " " "	0.001	Feels better—walks better.



July 27.	Intrasp. inj. salvarsanized serum	0.001	Urinary symptoms unchanged.
Nov. 13.	" " " "	0.001	On the whole improved, but still complains of weakness in legs.

1916 gm.

Apr. 13.	Intrasp. inj. salvarsanized serum	0.001	
Apr. 25.	" " " "	0.00075	Spinal fluid unchanged. 0.6-1.0 c.c. +++. Globulin 0. Cells 1. Blood Wassermann negative.

May 10. Lumbar puncture, saline lavage 30 c.c.

May 24. Saline lavage 30 c.c.

gm.

June 7.	Arsphenamine intrave. 0.3, intrasp. 0.001	Feels very good—stronger. Improving, but not well.
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July 5.	Arsphenamine intravenously	0.4 gm.	
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July 19.	" "	0.4 "	
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Oct. 4.	" "	0.3 "	
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Nov. 2.	" "	0.25 "	Spinal fluid 0.1-1 c.c. negative. Globulin +, 3 cells. Com- plains of difficulty in start- ing stream.
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Nov. 11.	Arsphenamine intravenously	0.4 gm.	Pain in back. Not so well. Still urinary difficulty.
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Nov. 23.	" "	0.35 "	Now feels better.
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Dec. 2.	" "	0.3 "	
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1917

Jan. 18.	Arsphenamine intravenously	0.3 gm.	Feels good. No sexual power. Urination now normal.
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Feb. 15.	" "	0.3 "	
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Mar. 20.	" "	0.35 "	Disease apparently arrested.
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May 17.	" "	0.3 "	
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June 26.	" "	0.3 "	Blood and spinal fluid nega- tive.
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This patient, a cerebrospinal luetic, was markedly benefited by the treatment he received and has remained subjectively well up to the present time. During the past year, up to July, 1918, he has received intravenous treatment as above about once a month. The disease is apparently arrested. The objective signs are unchanged.

On admission for treatment the spinal fluid was already negative up to 0.5 c.c. and with treatment became entirely negative. In cases of this type the biological reactions are apt to become progressively weaker and finally negative.

#### CASE 21

H. E., fifty years old, married, salesman. Was admitted for treatment on June 15, 1916, with a history of initial lesion thirty years before for which

he received only local treatment until some years later when he took occasional courses of mercury and K. I. internally. For the past six years has had severe pains down the legs and thighs; a girdle sensation about his lower chest, and a feeling of fullness in his abdomen. Recently he has had great difficulty in starting the urinary stream and has become impotent. He walks with some difficulty, especially at night, and can not continue his business of drumming the city trade.

*Physical Examination.*—Argyll Robertson pupils, absent knee and Achilles jerks; moderate Romberg; moderate ataxia of the legs; diminished sensation in the soles and dorsum of feet.

Blood Wassermann ++.

Spinal fluid positive 0.1-1 c.c. + + + +, 55 cells per c.mm., globulin +. Gold solution—syphilitic curve.

From June 18, 1916, to April 16, 1917, received 9 injections of arsphenamine intravenously, followed by rapid and progressive improvement in all the symptoms except the impotence. Spinal fluid showed 5 cells c.mm., a faint globulin reaction and positive Wassermann in 0.6 -1 c.c. + + + +.

In March and April, 1917, he was lumbar punctured four times, 30 c.c. of fluid removed and replaced by 15 c.c. of his own serum inactivated and non-medicated. The spinal fluid Wassermann became gradually and progressively weaker, in September being negative up to 2 c.c., contained 3 cells per c.mm., and the globulin showed a faint reaction. The blood was entirely negative. He felt quite well and had absolutely no pain; walked miles without difficulty; had a barely perceptible stiffness. The somatic signs of the disease were unchanged.

Case illustrating initial benefit serologically and subjectively derived from intravenous therapy. Further illustrating value of lumbar puncture and injection of normal serum intraspinally.

#### CASE 22

P. C., fifty-two years old, married, a drummer, admitted to the hospital March 10, 1916. History of initial lesion 32 years ago. His present trouble began three years ago with ptosis of left eye and diplopia, which condition was cured by his doctor by internal medication, but has recurred. He walks with the greatest difficulty and only very short distances. He has some pain in the legs, and marked diminution of sexual power.

*Physical Examination.*—Ptosis of left upper lid. Argyll Robertson pupils. External rectus weakness of the left eye. Absent knee and Achilles jerks. Marked Romberg. Marked ataxia and hypotonia.

Spinal fluid positive 0.1-1 c.c. + + + +. 56 cells to c.mm., globulin ++.

Blood Wassermann + + + +.

Received 12 injections of arsphenamine intravenously and was lumbar punctured five times, 30 c.c. of blood being withdrawn and replaced by normal serum. The Wassermann remained unchanged. The cell count was reduced to 11 cells per c.mm. There was marked improvement in the symptoms. The patient was able to walk better and also was able to resume his business of traveling about the city soliciting. After two more spinal punctures there was a further reduction in the cell count to 7 per c.mm. The Wassermann was positive from 0.4-

1 c.c. After four more spinal punctures and replacement by normal serum (inactivated) the cell count dropped to normal. The globulin reaction was negative. The spinal fluid in 1 c.c. was + positive (one-plus).

After an interval of three months and cessation of treatment, the Wassermann reaction again became positive from 0.1-1 c.c. and there were 50 cells to the c.mm., globulin +. The objective and subjective symptoms remained as before. Further intravenous injections plus lumbar puncture every other week gradually resulted in a negative fluid again after about six months treatment.

Illustrating the reduction of biological reactions to normal after intravenous treatment plus intraspinal injections of normal and salvarsanized serum with marked clinical improvement followed by a gradual return of all biological reactions but with apparent arrest of disease. The history and details of treatment are greatly abbreviated but this case represents one of the satisfactory results that can be obtained by patient and persistent therapy. In the course of treatment this patient became "sensitized" to the drug used (arsphenamine) and each injection had to be preceded by the subcutaneous administration of adrenalin (m. 10).

## CASE 23

B. M., thirty-seven years old, married, engineer. Came under treatment on January 30, 1916, with a history of chancre in 1908, for which he was treated 9 months by injections of Hg and three months with K. I. internally. No further treatment up to the present time. Married three years and has one healthy child.

Eight weeks ago complained of sudden severe stabbing pains in small of back radiating up to arm and down legs. No other symptoms.

*Physical Examination.*—Pupils react to light and accommodation. Right pupil slightly larger than left and slightly sluggish in reaction to light. Knee jerks active, Achilles present. No Romberg or Babinski. No ataxia.

Blood Wassermann ++ positive.

Spinal fluid ++++ 0.1-1 c.c., 50 cells c.mm., globulin ++.

1916		gm.
Feb. 2.	Arsphenamine intravenously	0.4.
Feb. 16.	" "	0.4.
Mar. 7.	" "	0.4. Pain abolished. Feels quite well. Pupils now almost equal in size and reaction.
April to June, 1916, Hg salicylate 0.06 gm. intramuscularly 12 times.		
1916		gm.
Sept. 16.	Arsphenamine intravenously	0.4.
Oct. 18.	" "	0.4.
Nov. 13.	" "	0.3.
1917		
Feb. 9.	Feels quite well. Occasionally slight pain in back. No more shooting pain at all. Wife has given birth to a healthy child.	

March to June, 1917, 12 injections of Hg salicylate (0.06 gm.) intramuscularly.

Oct. 10, 1917. Lumbar puncture.—Spinal fluid

{	0.1-0.9 negative.
	1.0 c.c. ++.
	0 cells.
	Globulin ±.

June, 1918. Patient has been under intermittent treatment since last October. His subjective and objective conditions are unchanged. He feels quite well. There is no relapse in the serologic reactions which are negative. The patient feels well and considers his condition cured.

#### CASE 24

L. H., thirty years old, married, salesman, was admitted to the hospital on February 16, 1915. Chancre and secondaries 8 years previously. Five years ago began to have sudden attacks of vomiting lasting four or five days. Attacks preceded by feeling of heavy load on abdomen for several days. Vomited 10 to 12 times daily during attack. No pain, but felt weak after paroxysms. Has had attacks about every two months now. For past nine months unsteady in walking especially in climbing stairs, and knees give way. Urinary incontinence for three months, and is impotent. No pains, girdle sensations, or paresthesia. Has had no treatment of any kind for the condition complained of or for syphilis.

*Physical Examination.*—Unequal pupils. React sluggishly to light on right side—left immobile. Knee and Achilles jerks absent. Cremasterics diminished. Romberg present. Slight hypotonia lower extremities. Moderate ataxia lower extremities. No intellectual deterioration detected.

Blood Wassermann test negative.

Spinal fluid Wassermann test 0.2 negative, 0.4-1 c.c. positive +++++. 10 cells c.mm., globulin 0.

Between February 18, 1915, and July 1, 1915, patient received seven intraspinal injections of salvarsanized serum, salvarsan being added to the serum in amounts up to 0.001 gram without reaction. Patient returned in August for his eighth injection and stated that his condition was decidedly worse. He received another treatment intraspinal in September, and although no local or general reaction followed immediately or within a few days of the injection, the patient for the first time commenced to complain of lightning pains in legs at intervals, increase in ataxia and increase in frequency of attacks of vomiting.

The spinal fluid became negative up to 1 c.c. after the 4th intraspinal treatment. At this time intravenous treatment was combined with intraspinal treatment. In all the patient received ten intraspinal injections and two intravenous injections up to November, 1915, but the subjective symptoms were decidedly worse. In 1916 patient was treated in the clinic by injections of mercury. He returned in April for an intravenous and intraspinal injection of mercurialized serum and then refused all further intraspinal injections because of the increase in subjective symptoms. Arsphenamine was administered intravenously thenceforth once or twice a month with occasional series of mercurial treat-

ments. Improvement was rapid and progressive and in the latter part of 1916 patient was able to return to work and has remained at work to date. The blood and spinal fluid are entirely negative.

Objectively a residuum of ataxia was noted although locomotion was good. Impotence remained. Urinary control was regained. The vomiting attacks have occurred at rare intervals since the beginning of intravenous treatment. It is to be noted that the spinal fluid reactions became rapidly negative under intraspinal therapy although the subjective improvement did not keep pace with the biological improvement, in fact, subjective symptoms were made decidedly worse, and the disease was progressive, as witness the advent of lightning pains.

## CASE 25

S. S., thirty-eight years old, married, clothing operator. Chancre ten years ago. For past four years has pains and numbness in feet and trouble with his vision. Ten days ago became almost blind and condition after lasting ten minutes cleared up. Has similar attacks daily. Is weak and walks with some stiffness. Decidedly weaker in right arm and can not work at trade of operator. Admitted to hospital Sept. 4, 1917.

*Physical Examination.*—(Sept. 5, 1917.) Pupils irregular, left greater than right, react to light. Slight ptosis right lid. Right internal rectus palsy. Left external rectus weakness. Right and left sup. rectus weakness. Right arm shows less power compared with left. Knee jerks active. Romberg present. Left Achilles absent. Left Babinski. Fundi—right posterior staphyloma.

Blood Wassermann + + + +.

Spinal fluid 0.1-1 c.c. + + + +, 20 cells c.mm., globulin +.

		gm.	
1917			
Sept. 20.	Arsphenamine	0.4	intravenously.
Oct. 22.	"	0.4	" " Lumbar puncture—
			Spinal fluid 2 cells c.mm.
			Globulin +.
			0.2 +.
			0.4 + + +.
			0.6-1 c.c. + + + +.
			Blood Wassermann + + +.
Oct. 25.	"	0.3	" "
Oct. 27.	"	0.3	" " Improving. Slight weakness left external rectus.
Nov. 30.	"	0.3	" " Lumbar puncture—Much better.
			Spinal fluid—0 cells.
			Globulin ±.
			0.1-0.8 neg.
			1 c.c. +.

The biological improvement has continued and patient in July, 1918, presents entirely normal reactions. Clinically however, patient shows only slight improvement. He has received treatment about twice a month, his general con-

dition is somewhat improved, but the essential symptoms of the disease have not as yet been materially changed. He is still unable to work.

## CASE 26

L. B., forty-three years old, married. Chancre 6 years ago. Admitted to the Hospital January 12, 1915, complaining of abdominal pains and urinary disturbance. Onset 15 months ago. After lifting heavy weight felt pain in back and girdle sensation in chest. Some trouble in starting stream noted. Operated on 9 months ago, in another hospital, for abdominal pains, and also received 5 intravenous injections of arsphenamine afterwards.

*Synopsis of Symptoms.*—Severe abdominal cramps in attacks lasting hours. Eructations and hiccoughs. Vomits occasionally (unrelated to meals). Urination difficult—occasional incontinence; constipation. Dull pain in back and legs. Girdle sensation in chest.

*Physical Examination.*—Pupils Argyll Robertson. Right K. J. absent, left diminished. Achilles absent. No ataxia—Romberg negative.

Blood Wassermann positive ++++.

Spinal fluid Wassermann +++++ 0.1-1 c.c., 45 cells, globulin ++.

1915 gram

Jan. 13. Arsphenamine 0.3 intravenously.

Jan. 15.

*Lumbar puncture*—20 cells per c.mm.

*Saline lavage* after removal 20 c.c. spinal fluid.

Jan. 22. Arsphenamine 0.3 intravenously.

Jan. 29.

*Lumbar puncture*—28 cells per c.mm.

*Saline lavage* after removal 30 c.c. spinal fluid.

Feb. 3.

Discharged. Unimproved. Still has gastric crises and vomits occasionally.

Apr. 24.

Readmitted. No better than when discharged in February.

15 c.c. salvarsanized serum intraspinaly 0.00025 gm.

July 14. 15 c.c. salvarsanized serum intraspinaly 0.0005 gm. No improvement.

Aug. 28. Normal (auto) serum intraspinaly 15 c.c. “ “

Oct. 5. 15 c.c. salvarsanized serum intraspinaly 0.001 gm. “ “

Nov. 11. 15 c.c. salvarsanized serum intraspinaly 0.001 gm. “ “

Dec. 10. 15 c.c. salvarsanized serum intraspinaly 0.001 gm. “ “

1916

Jan. 11. 15 c.c. salvarsanized serum intraspinaly 0.001 gm. “ “

Jan. 18. Arsphenamine 0.3 intravenously.

Jan. 25. “ 0.3 “

Feb. 15.	15 c.c. salvarsanized serum in-	No improvement.	
	traspinally 0.001 gm.		
Mar. 28.	15 c.c. salvarsanized serum in-		
	traspinally 0.001 gm.		
	Arsphenamine 0.3 intravenously.		
June 1.	Arsphenamine 0.3 intravenously.		
Aug. 23.	" 0.3 "		
Aug. 28.	" 0.25 "		
Aug. 30.	" 0.2 "		
Sept. 1.	" 0.2 "		
Sept. 6.	" 0.35 "		
Sept. 8.	" 0.4 "		
Sept. 13.	" 0.2 "		
Sept. 15.	" 0.2 "		
Sept. 18.	" 0.2 "	Clinical condition unchanged.	
Oct. 24.	" 0.3 "		
Oct. 31.	" 0.2 "		
Nov. 28.	" 0.3 "		
Dec. 7.	" 0.3 "	Lumbar puncture—116 cells, Wasser-	
		mann ++++ 0.1-1 c.c., globulin ++.	
Dec. 14.	" 0.4 "		
1917			
Jan. 2.	Arsphenamine 0.3 intravenously.	Condition unchanged.	
Jan. 9.	15 c.c. own serum intraspinally.	68 cells, spinal fluid Wassermann	
		++++ 0.1-1 c.c., globulin +.	
Feb. 27.	Arsphenamine 0.3 intraspinally.	Blood Wassermann +. Condition	
		slightly improved.	
Mar. 15.	" 0.3 "		
Mar. 19.	" 0.3 "	Condition about the same.	
April 10.	" 0.3 "	Lumbar puncture: 47 cells, Wasser-	
		mann sp. fl. ++++ 0.1-1 c.c., globu-	
		lin ±.	
		Condition improved.	

Referred to Montefiore Home clinically unimproved. Serologically—blood reduced to one-plus, spinal fluid unchanged after frequent and persistent intraspinal and intravenous injections.

Patient returned to Mt. Sinai Hospital in the spring of 1918. He received mercurial treatment at Montefiore and in the clinic at Mt. Sinai. He was admitted to the hospital and intravenous treatment with arsphenamine given every 2 to 4 weeks instituted. Patient is still complaining of symptoms similar to those present at time of admission. In spite of numerous intravenous and intraspinal injections together with innumerable injections of mercury and much KI internally the biology of the latter is unchanged. There is no evidence of general paresis. The gold curve is a luetic one.

#### CASE 27

H. R., thirty-eight years old, married, was admitted December 20, 1913, with a history of initial lesion in 1904 for which he was treated for 7 months by pills

DATE	INTRAVENOUS TREATMENT	INTRASPINAL TREATMENT	REMARKS	SEROLOGY
1/ 4/14	Arsphenamine 0.3	0	Much improved	Sp. Fl. ++++
12	" 0.3	0	can walk	0.1-1 c.c.
21	" 0.3	0	without aid.	Globulin +.
4/ 7/14	" 0.3	0	Ataxia almost gone. Enuresis better.	Cells 13. Blood ++++.
4/24/15		15 c.c. salvarsanized serum 0.00025 gm.	Ataxia again. No treatment in one year; now quite ataxic.	
5/19/15		15 c.c. salvarsanized serum 0.0005 gm.	Shooting pains legs.	Same as above, 4 cells.
6/ 2/15		15 c.c. salvarsanized serum 0.0005 gm.	Gait stiff, pains legs.	++++ 0.1-1 c.c. 4 cells, Globu- lin +.
6/18/15		15 c.c. salvarsanized serum 0.00075 gm.		
7/ 8/15		15 c.c. salvarsanized serum 0.00075 gm.		
8/24/15		15 c.c. salvarsanized serum 0.001 gm.	Urinary symp- toms unim- proved.	Sp. Fl. ++++ 0.1-1 c.c., 6 cells, Globu- lin ±.
10/23/15	Arsphenamine 0.3 gm.	15 c.c. salvarsanized serum 0.001 gm.		Blood ++++.
11/25/15		15 c.c. salvarsanized serum 0.001 gm.	Less pain. Feels better.	
5/ 5/16		15 c.c. salvarsanized serum 0.00075 gm.		
5/19/16		15 c.c. salvarsanized serum 0.001 gm.		
6/12/16		15 c.c. salvarsanized serum 0.001 gm.		
7/ 8/16		15 c.c. salvarsanized serum 0.001 gm.		
8/24/16		15 c.c. salvarsanized serum 0.001 gm.	Condition unim- proved, incont- inence, pain legs, spastic- ity.	
9/20/16	Arsphenamine 0.3	15 c.c. salvarsanized serum 0.001 gm.		
9/25/16				
10/31/16	Arsphenamine 0.3		Spasticity con- tinues. Pain less.	
10/14/16	" 0.3			
10/17/16	" 0.3			
11 14/16	" 0.3	Lumbar puncture 10 c.c.		
12/ 5/16	" 0.45			
12/12/16	" 0.3			
12/19/16	" 0.3			
12/26/16	" 0.3			
1/ 2/17	Arsphenamine 0.3			
1/ 9/17		Normal serum 15 c.c.		Blood ++++
2/ 8/17		Salvarsanized serum 0.00025 gm.		Sp. fl. 20 cells, Globu- lin +, 0.1-1 c.c. ++++.
3/ 1/17	Arsphenamine 0.3+	Salvarsanized serum 0.0005 gm.		
3/15/17	" 0.3			
4/14/17	" 0.4	Normal serum 15 c.c.		
6/19/17	" 0.3	0		
7/26/17	" 0.3	0	Condition grad- ually progres- sive.	



and inunctions. Has three healthy children. Wife never had any abortions. Chief complaint is lancinating pains down legs for nearly 5 years, gastric crises and occasional incontinence.

*Physical Examination.*—Thin, not well nourished. Pupils irregular, right greater than left. No reaction to light or accommodation. Marked ataxia left lower extremity. Left K. J. absent, right present. Achilles both absent. Romberg slight. No Babinski. Gait ataxic—slightly spastic. Sensations normal.

Blood positive ++++ Wassermann.

Spinal fluid Wassermann—0.1-1 c.c. ++++ positive, 13 cells, globulin 0.

	1914	gram	
Jan. 4.	Arsphenamine	0.3	intravenously.
Jan. 12.	"	0.3	" Enuresis now better.
Jan. 21.	"	0.3	" Gait better; can walk without support. Ataxia almost gone. General condition better. Left hospital.
Apr. 7.	Arsphenamine	0.3	intravenously. Readmitted with recurrence of ataxia. Blood Wassermann ++++ positive. Spinal fluid ++++ positive 0.1-1 c.c., 4 cells, globulin 0.

Intraspinal treatment was persisted in until the latter part of 1917. The lesion was progressive, the symptoms unimproved, the patient's general condition unimproved. Treatment with Hg and KI was interspersed with the above throughout the entire period. Patient was advised to take a long rest and vacation. He returned in September, 1918 unimproved. His lesion involves the lateral tract with an increase in spasticity, positive Babinski, as well as the posterior aspect of the cord. Mentally he is quite well. There is no evidence of general paresis; the gold curve is negative. All forms of treatment, including repeated intraspinal injections, have been of no avail.

#### CASE 28

E. R., thirty-two years old, married, contracted syphilis seven years ago, in February, 1911. He first came under treatment after the development of the secondary roseola. Treatment for the first year consisted of one intramuscular injection of salvarsan 0.6 gram in iodipin followed by 15 intramuscular injections of mercury salicylate (gr. 1 to 2) after which an intravenous injection of arsphenamine (0.6 gram) was administered. No further treatment was taken until one year later, March, 1912, at the beginning of the second year of the disease a second intravenous injection of arsphenamine (0.6 gram) was given followed by twelve injections of calomel intramuscularly, and in November, 1912, he again received an intravenous injection of arsphenamine (0.6 gram). During 1913, in the third year of the disease the patient received three courses, 36 injections, of mercurial injections (salicylate).

During 1914 the fourth year of the disease the patient's visits and treatments were irregular, and he received in all about a dozen injections of mercury salicylate. During this year a healthy child was born to the wife of this patient who

was also infected about the same time the patient first showed manifestations of the disease, but in whom the blood Wassermann had become negative.

During 1915 and 1916, the fifth and sixth years of the disease respectively, the patient received in all three injections of arsphenamine intravenously and two courses of mercury injections each year.

With the rapid decline of the roseola under the arsphenamine (intramuscularly), as it was then administered, and the subsequent injections of mercury, the subjective symptoms of early lues and all objective signs disappeared. The patient has never had a return of any of the manifestations of the disease and has felt quite well. The Wassermann reaction in the early secondary period (February, 1911) was positive + + + +, and in spite of continuous treatment of as intensive a nature as the patient's circumstances permitted remained persistently positive with slight variations in intensity.

During 1917 the patient received 6 intravenous injections of neoarsphenamine but declined injections of mercury. The iodide of potash in increasing doses was taken twice this year. The reaction in the blood remained positive and inasmuch as no subjective and objective symptoms were present the patient declined lumbar puncture.

In January, 1918, a lumbar puncture was insisted upon on account of the persistence of the blood reaction. The fluid was found definitely positive from 0.1 c.c. upwards, there were 55 cells to the c.mm., and the globulin was increased.

In the absence of subjective or objective symptoms referable to the nervous system, but in view of the positive biological reactions, intensive treatment intravenously was begun in January, 1918, and the patient received fourteen injections of arsenobenzol in a period of about 11 weeks followed by mercury salicylate intramuscularly and iodide of potash by mouth. A repetition of the lumbar puncture has not been permitted on account of the severe symptoms following the first puncture which kept the patient in bed a week, the headache lasting even longer.

Aside from a slight sluggishness of one pupil there are no objective signs of nervous involvement, although the occasional occurrence of slight paraesthesia sensations in one thigh may be heralding the approach of root involvement. The blood is still positive. There are no signs of intellectual deterioration.

#### CASE 29

D. S., thirty years old, single, was admitted to the hospital on December 22, 1915, with a history of initial lesion 12 years previously.

Six weeks ago, after exposure to cold, noticed a heaviness and weakness, first in the right leg and a little later in the left lower extremity. He walked with difficulty on account of stiffness in the legs. His Wassermann was found + + + + by his physician who put him on injections of mercury. He improved rapidly and after 10 injections could walk without discomfort. There was still some spasticity, however, especially of the right leg.

*Physical Examination.*—Pupils irregular, but react to light and accommodation. Knee jerks and Achilles exaggerated. Bilateral Babinski. Loss of

deep sensibility of the legs. Slight Romberg. Gait spastic. Right leg held rigid.

Blood Wassermann ++++ positive.

Spinal fluid Wassermann 0.1 to 1.0 c.c. negative, globulin negative, cells 0.

From December 22, 1915, to December 23, 1916, the patient received eleven injections of arsphenamine with marked improvement in his condition, although his gait remained somewhat spastic. There was no change in the blood which remained ++++. The spinal fluid was negative.

Two weeks after the last treatment there was a sudden onset of extreme spasticity in the legs so that the patient could not leave his bed. The spinal fluid was under greatly increased pressure, but was negative in all of its reactions including the gold solution reaction. The blood was positive ++++.

After intensive arsphenamine treatment over a period of two months the spasticity again improved so that the patient was able to walk. Soon after the cessation of treatment, in May, 1917, the patient having regained the power to walk, although there was still some spasticity, there was a sudden onset again of extreme spasticity. The patient was unable to leave his bed although in every other respect he felt entirely well.

Under persistent intravenous therapy combined with re-education and local treatments for the relief of the spasticity and correction of contracture, the patient is gradually improving. Spinal fluid reactions are repeatedly negative. Last blood test positive ++++.

This case represents one of a group of cases showing progressive invasion in spite of fairly intensive treatment and in the presence of entirely negative serologic reactions in the spinal fluid.

#### CASE 30

B. H., thirty-five years old, chauffeur, was admitted to the hospital March 17, 1916, with a history of initial lesion 16 years ago, for which he had received 15 injections of salvarsan and a similar number of injections of mercury in the course of the past five years. The last treatment was received six months before admission. Ten days before admission to the hospital, and after exposure to cold, felt a sudden weakness and stiffness in both legs. The stiffness has increased and the legs feel "numb." He has difficulty in starting the urinary stream.

*Physical Examination.*—Pupils irregular, react sluggishly to light and accommodation. Knee jerks exaggerated. Ankle clonus present. Positive bilateral Babinski. Romberg positive. Marked spasticity in both lower extremities.

Blood Wassermann positive ++.

Spinal fluid 0.1-1 c.c. positive ++++, 112 cells to c.mm., globulin ++.

The patient received one injection of arsphenamine intravenously and four injections intraspinaly of mercurialized serum containing respectively 1/100 to 1/50 of a grain of  $\text{HgCl}_2$ . After the third injection, which represented a lapse of about two months' time, the spinal fluid was 0.6 c.c. ++; 0.3 to 1.0 c.c. ++++ positive; 12 cells, globulin trace.

The patient received three more injections of arsphenamine intravenously

and another intraspinal injection of mercurialized serum containing 1/50 grain of bichloride of mercury. The injections were all well borne. After the last treatment the spinal fluid Wassermann was still positive in 1 c.c. only. The cell count and globulin were normal.

The clinical condition, however, showed no material change. There was still marked spasticity of both lower extremities, some pains in the legs, and a loss of bladder control. Six months later the patient returned to the hospital stating that the gait was still spastic so that he was unable to pursue his occupation of chauffeur any longer. The spinal fluid was negative in one c.c. now. No cells, globulin negative. Blood Wassermann negative.

After three more intravenous injections of arsphenamine the patient improved somewhat. The spinal fluid was entirely negative in all its reactions. The patient received eight injections of mercurialized serum, intraspinally without further benefit.

The case illustrates the progression of lesion and symptoms with a diminution in all the biological factors both in the spinal fluid and blood in spite of intensive intraspinal treatment (mercurialized serum intraspinally, plus intravenous arsphenamine injections).

#### CASE 31

N. A., forty-one years old, single, salesman, acquired lues 20 years ago. Chancre on penis followed by secondary eruption. Received only a brief course of internal mercurial medication during the first year. One year ago had an attack of pneumonia and about a month later suddenly developed a right-sided hemiplegia with aphasia. The aphasia has improved considerably as has the hemiplegia.

Blood Wassermann test was found positive soon after onset of trouble.

*Physical Examination.*—Right-sided hemiplegia. Right arm spastic with hyperactive reflexes and marked ataxia, and loss of power. Right lower extremity dragged in walking and similarly hypertonic with all reflexes markedly exaggerated. Positive Babinski, Oppenheim, positive ankle and patellar clonus. Loss of postural sense. Abdominals active. Pupils equal and react to light and accommodation. No ocular palsies. No evidences of renal, cardiac or pulmonary involvement. Blood pressure normal.

Blood Wassermann test faintly positive.

Spinal fluid under increased pressure. Wassermann test negative 0.1-1 c.c., globulin ++, cells normal.

Sensory aphasia very evident. No definite change following a number of injections of arsphenamine intravenously.

This patient has been under treatment for a number of months, but the destruction due to vessel closure or slight hemorrhage is permanent. There is no improvement. This is possibly a case of postpneumonic embolism in a luetic individual.

#### CASE 32

A. T., twenty-six years old, acquired syphilis six years ago. Treatment was begun soon after the development of the secondary rash and consisted in a few injections of arsphenamine followed by mercury by mouth. In the past six

years he has received in all ten injections of arsphenamine intravenously. For the past year or so he has not felt well; he has been weak and nervous, unable to keep up his clerical work and for any length of time, has an almost constant headache, and is very depressed and gloomy. During the past few months has noticed the gradual onset of weakness in right arm and leg.

*Physical Examination.*—General condition only fair, looks worried and depressed and is anemic. Leucoplakia angles mouth and sides cheek. Pupils react to light and accommodation. No ocular palsies. Right knee jerk and Achilles somewhat hyperactive. Right upper extremity somewhat hypertonic. Slight spasticity in right arm and leg. No definite ataxia. Right Babinski. No sensory changes. Gait shows some spasticity in right leg and arm is held in constrained position. Power in both arm and leg diminished.

Blood repeatedly negative Wassermann reaction.

Spinal fluid negative—0.1 to 2 c.c., 0 cells, globulin 0, gold solution negative.

Treatment in this case has of necessity been irregular. He has received an intravenous injection every other week of arsphenamine 0.4 gram. He returns for treatment in September, 1918, stating that he is much stronger and feels able to do some work. Is working regularly as clerk at end of October, 1918.

#### CASE 33

S. B., thirty-eight years old, an orderly, was admitted to the hospital on November 20, 1916, with a history of stiffness and pains in both legs for four months, incapacitating him from working. Left leg is especially weak and gives way at the knee when he attempts to stand on it for a long time. Some paresthesia left leg. Some loss of control of urination for a year. Is not able to work.

*Physical Examination.*—Irregular pupils which react sluggishly to light and accommodation. Left leg stiff and is dragged on walking. Some ataxia in leg and also in left arm. Area of hyperalgesia in sacral segments. Right abdominal reflexes absent. Cremasterics sluggish. Knee and Achilles jerks on both sides sluggish.

Blood Wassermann reaction negative.

Spinal fluid Wassermann negative 0.1-1 c.c., 0 cells, 0 globulin.

1916	gram
Nov. 28. Arsphenamine	0.3 intravenously.
Dec. 2.           "       "	0.3       "
Dec. 5.           "       "	0.4       "
Dec. 9.           "       "	0.35      "

Markedly improved by this treatment. Pain gone and stiffness much less marked. Returns for further treatment.

1917	gram
Mar. 17. Arsphenamine	0.4 intravenously.
Apr. 5.           "       "	0.4       "
Apr. 21.          "       "	0.4       "
May 12.          "       "	0.3       "
May 31.          "       "	0.3       "

June 21. Arsphenamine 0.35 intravenously.

July 14.	"	0.35	"	Much improved.	Occasionally some
July 28.	"	0.4	"	pains in legs.	
Sept. 29.	"	0.4	"		
Oct. 25.	"	0.4	"		
Dec. 1.	"	0.4	"		
Dec. 20.	"	0.4	"		

This cerebrospinal luetic gave entirely negative serological findings both in the blood and spinal fluid. Treatment was entirely effectual in removing almost entirely the subjective symptoms.

Improvement in gait and station also marked so that patient is again able to pursue his usual vocation successfully and has been at work steadily since his last treatment.

#### CASE 34

K. D., thirty-four years old, single, denies infection with lues. Was admitted April 18, 1917, complaining of paresthesia in lower extremities, severe, sharp shooting pains in legs, back and abdomen. Girdle sensation about lower chest, and occasional attacks headache and dizziness for about four years. One year ago had incontinence of urine for a time but this has disappeared. Some time ago his blood Wassermann was reported positive by his physician and he received four injections of arsphenamine intravenously and six injections of neoarsphenamine also intravenously.

*Physical Examination.*—General condition fair. Pupils pinpoint—Argyll Robertson. Fundi negative. No ocular palsies. Abdominal reflexes active. Knee and Achilles jerks active.

Blood Wassermann negative.

Blood Wassermann after provocative two-plus positive (++) .

Spinal fluid Wassermann 0.1-1 c.c. negative, 0 cells, 0 globulin.

After a number of intravenous injections of arsphenamine followed by mercury intramuscularly the subjective symptoms were markedly improved. The biological reactions in the fluid were and remained negative. This patient is still under treatment though quite well and able to work.

#### CASE 35

A. A., thirty-eight years old, widow, was admitted on July 3, 1916, with a history that up to six years previously was perfectly well. She had one healthy child and no miscarriages. First husband was luetic. Six years ago a physician diagnosed a skin condition as syphilitic and upon receiving two injections of arsphenamine the lesions disappeared. Three years afterwards patient began to have severe headaches and double vision appeared. After two injections of arsphenamine these symptoms disappeared. About 8 months after this time urinary incontinence developed and has persisted for about two years up to the present time. Patient has received considerable mercurial and arsphenamine treatment without apparent benefit.

*Physical Examination.*—Pupils are equal and react sluggishly to light and accommodation. No ocular palsies. Fundi negative. Extremities show no

ataxia. Romberg negative. Right Babinski present. Right Achilles greater than left. Abdominal reflexes present. General condition good. Bladder negative (cystoscopically). Anterior and posterior vaginal walls relaxed, not sufficient, however, to account for incontinence. Patient is of a more or less neurotic make-up. No intellectual deterioration evident.

Blood Wassermann negative.

Spinal fluid Wassermann negative 0.1-1 c.c., 0 cells, 0 globulin.

1916		gram	
July 7.	Arsphenamine	0.3	intravenously.
July 14.	"	0.3	"
July 19.	"	0.3	"
July 21.	"	0.3	"
Aug. 17.	"	0.3	"
Aug. 21.	"	0.35	"
Sept. 13.	"	0.3	"
Sept. 25.	"	0.35	"
Oct. 2.	"	0.3	"
Oct. 4.	"	0.3	"
Oct. 21.	"	0.3	"
			Very much better. Holds urine all night.
			Improved—occasional loss urine.
			Feels worse—very nervous on account of family troubles, can not hold urine.
Nov. 4.	"	0.4	"
Nov. 11.	"	0.4	"
Nov. 18.	"	0.3	"
1917			
Jan. 13.	Arsphenamine	0.25	intravenously. Some pain and stiffness in lower extremities. Urinary control better.
Feb. 6.	"	0.25	"
Feb. 3.	"	0.3	"
Feb. 27.	"	0.3	"
			Pain substernal—deep—some impairment vision. Fundi negative.
			Some pain in knees—headaches—pupils react somewhat more sluggishly though equally.
Mar. 8.	"	0.3	"
Mar. 13.	"	0.3	"
Apr. 5.	"	0.3	"
Apr. 19.	"	0.3	"
Apr. 26.	"	0.3	"
May 8.	"	0.3	"
May 22.	"	0.3	"
May 31.	"	0.3	"
June 14.	"	0.3	"
July 17.	"	0.3	"
July 26.	"	0.3	"
Sept. 4.	"	0.3	"
Sept. 20.	"	0.35	"
Oct. 9.	"	0.3	"
Oct. 20.	"	0.3	"
			Much improved. No complaint now.

Nov. 3. Arsphenamine 0.3 intravenously.

Nov. 27. " 0.3 "

Dec. 6. " 0.3 " At work regularly.

Much better; little pain if any and unless under great emotional strain, feels well and holds urine at all times. Has been getting occasional mercurial treatment in intervals between visits for arsphenamine injections.

Blood and spinal fluid always negative. Practically no change in somatic signs.

#### CASE 36

J. S., forty-seven years old, tailor, admitted July 25, 1916, with a history of chancre 30 years ago. For past two years has had headaches and pain in right hypochondriac region and cold sensation in legs. Has been impotent for three years. Has been unable to work on account of leg condition.

*Physical Examination.*—Pupils normal—react to light and accommodation. Reflexes normal. Knee and Achilles jerks present. Bilateral Babinski. Slight left ankle clonus.

Blood Wassermann negative.

Spinal fluid Wassermann 0.1-1 c.c. negative, 50 cells per c.mm., globulin ++.

1916	gm.	
July 29.	Arsphenamine 0.3 intravenously.	
Aug. 4.	" 0.4 "	
Aug. 6.		Lumbar puncture—Wassermann test negative, 38 cells, globulin +.
Aug. 7.		All pains entirely cured. Feels much better.
Aug. 11.	Arsphenamine 0.3 intravenously.	
Aug. 15.	" 0.3 "	Blood Wassermann negative.
Aug. 21.	" 0.35 "	
Aug. 23.		Lumbar puncture—Wassermann reaction 0.1-1 c.c. negative, globulin +, 11 cells.
Sept. 1.	Arsphenamine 0.4 intravenously.	Feels fine—better than in years.
Sept. 8.	" 0.4 "	
Oct. 24.	" 0.3 "	Feels good—slight difficulty in voiding urine and some coldness in extremities.
Oct. 31.	" 0.3 "	
Nov. 14.	" 0.4 "	
Dec. 12.	" 0.4 "	Blood Wassermann now one-plus positive (+).
Dec. 16.	" 0.3 "	Blood Wassermann now two-plus positive (++). Lumbar puncture—Spinal fluid Wassermann negative 0.1-1 c.c., 7 cells, globulin ++.



1917		gm.		
Jan. 16.	Arsphenamine	0.3	intravenously.	Blood Wassermann now positive +++.
				Now has complete urinary control.
Feb. 4.	"	0.3	"	Thinks he is completely cured. Urinates normally and coldness in extremities much better.
Feb. 18.	"	0.3	"	

The Wassermann test of the blood was repeatedly negative before and for almost six months after the beginning of antisyphilitic treatment. Only after repeated injections did the reaction gradually and in stages become positive in the blood. In spite of negative biological findings with the exception of the pleocytosis in the fluid, the subjective symptoms yielded promptly and completely to antisyphilitic treatment. The patient was able to return to work and felt better than in years shortly after the first few weeks of intensive treatment.

## CASE 37

K. G. fifty-five years old, engineer, acquired lues thirty years previously for which he received mercury and iodide of potash by mouth and occasionally during the past decade an occasional course of injections of mercury bichloride. For the past few years he has had occasional attacks of tingling sensations in feet and sharp pains in both lower extremities. His urination has become increasingly more difficult and for more than a year he has become impotent though the libido is strong.

*Physical Examination.*—Typical tabetic with Argyll Robertson pupils. Absent knee and Achilles jerks. Marked Romberg. Marked ataxia in both lower extremities. Irregularly distributed anesthetic and hyperesthetic areas in both feet. Marked hypotonia. Bladder shows retention with marked trabeculation of bladder wall.

Blood Wassermann negative.

Spinal fluid Wassermann 0.1-1 c.c. negative, 3 cells, 0 globulin.

In this tabetic the institution of treatment caused some amelioration of symptoms. Objectively there was no change. In spite of the fact that the lesion was active and more or less progressive the biological reactions in this case were repeatedly negative.

## CASE 38

K. M., fifty-five years old, a traveling salesman, was referred to us on account of neuritic pains in both legs and in the back. For a number of years he had been treated by physicians for "neuritis" and "rheumatism." The pain complained of was like a "toothache" and was only occasionally present in both calves and thighs, and was worse in stormy weather. There were no other symptoms.

Physical examination revealed a typical *tabes dorsalis*. There was an absence of both pupillary reactions to light but a prompt reaction to accommodation. Both knee and Achilles jerks were absent. The cremasterics were sluggish

There were scattered areas of anesthesia in both lower extremities. There was no evidence of hypotonia or ataxia. Gait was normal; no change in station.

The blood showed a strongly positive (++++) Wassermann reaction. The spinal fluid was positive (++++) in the lowest dilution tested, 0.1 c.c. There were 155 lymphocytes to the cubic millimeter. The globulin reaction was positive (++) . Gold solution—syphilitic curve.

The patient was treated every five days with arsphenamine intravenously (0.4 gram) for eight injections, followed by a course of twelve injections of mercury salicylate intramuscularly within two months. At the expiration of the first month all subjective symptoms were abolished. The patient is free of all symptoms, goes about his work necessitating long walks without difficulty. The blood is now negative. Lumbar puncture has not yet been repeated. The symptoms in this case were present for years without apparent progression of the lesion without any treatment. There was no history of lues by name or symptoms.

#### CASE 39

F. G., twenty-six years old, dentist, was admitted to the hospital in October, 1917, on account of a positive Wassermann reaction in spite of persistent treatment. He acquired a chancre four years before admission which was followed by a roseola and then treatment was instituted by his physician. He received in all 13 injections of arsphenamine intravenously in full doses (0.6 gram) and injections of Hg salicylate and potassium iodide in alternating periods. He has no complaint to offer but is worried because his blood fails to become negative.

*Physical Examination.*—General condition excellent. Pupils react to light and accommodation but are somewhat irregular and the right pupil is somewhat dilated. All reflexes normal—superficial and deep. No Babinski. No bladder symptoms. No ataxia.

Blood Wassermann positive ++.

Spinal fluid Wassermann positive 0.1-1 c.c. +++, 300 cells c.mm., globulin +.

1917	gm.
Oct. 25.	Arsphenamine 0.4 intravenously.
Oct. 27.	“ 0.3 “
Nov. 1.	“ 0.5 “
Nov. 10.	Normal serum (50%) inactivated 15 c.c. <i>intraspinally</i> . Very severe reaction.

Spinal fluid Wassermann 0.1-1 c.c. +++, 80 cells c.mm., globulin +.

Blood negative.

1917	gm.
Dec. 2.	Arsphenamine 0.4 intravenously.
Dec. 5.	“ 0.4 “
Dec. 10.	“ 0.4 “
Dec. 19.	“ 0.4 “

*January to March, 1918,* Hg salicylate gr. 1 to 2 every 5 days.

*March 17, 1918.* Blood Wassermann reaction negative. Feels fine. No subjective or objective change.

May 4, 1918. *Lumbar puncture*—Spinal fluid Wassermann positive 0.1-1 c.c. + + + +, 75 cells c.mm., globulin 0.

The blood Wassermann has become negative. The spinal fluid reactions persist showing an active meningeal process but there are absolutely no subjective symptoms or objective signs other than the specific pupils. There is no sign of intellectual deterioration. On account of the repeated attacks of "aseptic" meningitis lasting from seven to fourteen days following lumbar puncture on two previous occasions, patient is reluctant to permit frequent tapplings or any form of intraspinal therapy. He has, however, received 8 more injections of arsphenamine intravenously and is under periodic observation and treatment.

## CASE 40

H. C., forty years old, married, admitted June 15, 1916, complaining chiefly of a band-like constriction about the chest and abdomen for about six months. Has some headaches, occasionally feels dizzy, and the least exertion causes a feeling of extreme weakness. Pain in left foot and leg occasionally, chiefly at night. Speech slow, stammering and hesitant, suggestive of general paresis. Gait somewhat uncertain and slow.

*Physical Examination.*—General condition fairly good. Pupils do not react to light, slightly to accommodation. K. J. and Achilles absent. Romberg positive. Gait stiff—somewhat ataxic.

Blood Wassermann + + + + positive.

Spinal fluid 0.1-1 c.c. + + + +, globulin + +, 110 cells.

	1916	gm.	
June 15.	Arsphenamine	0.3	intravenously.
July 25.	"	0.3	" Anaphylactoid reaction immediately after arsphenamine.
Aug. 1.	"	0.3	" Gait somewhat improved—girdle still present.
Aug. 15.	"	0.3	" Feels much better—able to work again.
Sept. 7.	"	0.3	" Complains of girdle sensation about waist, chest and right leg.
Sept. 14.	"	0.3	" Left Babinski noted—gait improved.
Oct. 4.	"	0.3	"
Oct. 19.	"	0.3	" Lumbar puncture, 0.1-1 c.c. + + + + positive, globulin +, 6 cells c.mm.
Nov. 28.	"	0.3	" Walks better. Still girdle sensation. Memory poorer. Suspicion of general paresis.
Dec. 7.	"	0.3	" Lumbar puncture—0.1-1 c.c. + + + +, globulin + +, 57 cells c.mm.
Dec. 14.	"	0.3	"
Dec. 21.	"	0.3	" Condition about same. Some spasticity of legs; a bit talkative.
Dec. 28.	Normal (auto) serum intraspinally 15 c.c. begun.		

	1917	gm.	
Jan. 10.	Arsphenamine 0.3 intravenously.	Not much change since above.	Says ataxia is worse.
Jan. 30.	" 0.3 "		
	Normal serum intrasp. 15 c.c.	Spinal fluid 0.1-1 c.c. ++++, 46 cells, globulin +.	Blood Wassermann ++++.
	gm.		
Feb. 9.	Arsphenamine 0.25 intravenously.	Walks more uncertainly since intra-spinal injection.	Thinks he is worse.
Mar. 15.	" 0.3 "		
Mar. 24.	" 0.3 "	No improvement.	
	Normal serum intrasp. 15 c.c.		
	gm.		
Apr. 7.	Arsphenamine 0.3 intravenously.		
Apr. 28.	" 0.3 "		
May 19.	" 0.3 "		
June 19.	" 0.2 "		
	Normal serum intrasp. 15 c.c.	Spinal fluid—0.2 negative, 0.4-1 c.c. ++++, globulin $\pm$ , 98 cells.	
July 28.	Arsphenamine 0.3 intravenously.	Feels much worse. Ataxia very marked. Can not walk alone. Mental condition worse. Complains a great deal, but no mental deterioration. Occasionally wets bed at night.	
Aug. 27.		Lumbar puncture—39 cells c.mm.	
Sept. 18.		Lumbar puncture—0.6 + 0.8-1 c.c. ++	
		Almost complete paralysis of legs. Very irritable mentally. Refuses further treatment.	

This patient gradually deteriorated and the diagnosis of general paresis was justified. In spite of the increase in the subjective and objective signs of the disease, the serologic reactions gradually showed improvement and suddenly became entirely negative in the spinal fluid. The blood remained positive.

#### CASE 41

M. K., forty-six years old, married, denies infection with syphilis. Was admitted to the hospital in April 7, 1917, after many months of treatment in dispensaries on account of urinary incontinence and impotence. He has complained of inability to control his urine especially at night for nearly ten years, and for the past few months he has had to urinate frequently by day and if the opportunity to empty his bladder was not present, the urine dribbled away. He has some pains in both lower extremities, occasionally lightning-like in character coming and going. He is somewhat weak, does not hear very well and complains of

tremor of both hands. His blood has been examined frequently and always found negative.

*Physical Examination.*—General condition fair—rather florid complexion. Pupils irregular, right greater than left. Right reacts to light, left immobile to light. Both react to accommodation. Both ears show chronic thickening drums. Abdominal reflexes active. Cremasterics present. Upper extremities—reflexes normal, slight tremor hands present. Lower extremities—knee and Achilles jerks present and equal. Left fundus shows distinct post neuritic atrophy optic nerve. Moderate neuritis right optic nerve.

Blood Wassermann negative.

Spinal fluid Wassermann 0.1-1 c.c. positive + + + +, 54 cells, + globulin.

This patient was treated intensively intravenously for a few weeks, and then left the hospital to return for treatment about twice a month. In the interim he obtained mercurial injections and treatment for his bladder condition by sounds, electricity, etc., in the clinic.

The biological reactions in the spinal fluid very rapidly disappeared, and in December, 1917, were entirely negative. This was achieved by intravenous injection of arsphenamine combined with mercury and an occasional tapping of the spinal canal, about once a month. The subjective improvement has been slow and the patient is still suffering with occasional periods of incontinence. The pains are slight and very infrequent.

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## SYPHILITIC MENINGITIS IN INFANTS AND YOUNG CHILDREN WITH REPORT OF A CASE

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THE paucity of reported cases of syphilitic meningitis in infants and young children lends interest to each additional one. The similarity of the clinical picture to that of tuberculous meningitis, and the frequent negative microscopic and serologic findings in the examination of the spinal fluid, make the diagnosis difficult; especially, when the family and antecedent histories are vague and unreliable. Hutinel<sup>1</sup> says that the reactions in syphilitic meningitis may resemble tuberculous meningitis or they may be insidious or latent. Inherited syphilis should be suspected when the meningitis does not present the classical picture of ordinary meningitis, and when the stigmata of hereditary syphilis are suggested. Spirochetes are not generally found in the spinal fluid, and the Wassermann reactions in blood serum and spinal fluid are often negative, becoming positive after recovery. He considers that syphilitic meningitis is part of a general septicemic disease in the first few weeks of life, but after two years of age, the meningeal symptom-complex is a lighting up of old reactions on the part of the already damaged nerve cells. The therapeutic test is conclusive.

This interesting corollary presents itself: In how many children, exhibiting a train of mild meningeal symptoms, is syphilis the etiological factor, and in how many is the cause unrecognized and, therefore, improperly treated?

In children, lumbar puncture is simple and, if carried out under strict aseptic precautions, is harmless. Vigorous mercurialization for a few days will often transform a negative Wassermann reaction into a positive one.

Lavergne<sup>2</sup> reports two cases of syphilitic meningitis in children of three and one-half and nine years respectively, in which the meningeal symptoms were attributed, solely, to syphilis. In the former, the Wassermann reaction was positive both with blood se-



rum and spinal fluid. There was a strongly positive cutaneous reaction. In the latter case, the Wassermann reaction was negative with blood serum, but positive with spinal fluid. There was a constant lymphocytosis of varying degree. Under specific treatment, the meningeal symptoms promptly disappeared. In the case of the younger child, a circinate eruption appeared four months later. In two other cases, with marked meningeal symptoms, and positive Wassermann reactions, the causes were doubtful. In one, there was a frank pneumonia, while poliomyelitis was suspected in the other. However, immediate improvement followed the administration of mercury.

Leitch<sup>3</sup> describes a case of acute meningitis in an infant of twelve months, which seems to be the youngest so far recorded. The initial symptoms were vomiting, constipation, and increasing drowsiness. In spite of negative tuberculin skin tests, and diligent search for the tubercle bacillus in the spinal fluid, it was still held to be probably tuberculous in origin. In searching for choroid tubercles, syphilis as the etiologic factor was first considered. There was no history of fever or convulsions. The spinal fluid was slightly turbid, containing 600 cells per c.mm. A centrifuged specimen showed the presence of numerous spirochetes. At necropsy, spirochetes were demonstrated in a grayish white exudate covering the blood vessels in the sulci of the parietal and temporal lobes. Other organs, especially the liver, showed signs of hereditary syphilis. The spinal fluid was negative for bacteria, both by smear and culture.

Vasiliu<sup>4</sup> observed three children of three, two, and three years, respectively, in whom a diagnosis of tuberculous meningitis had been made, who presented the stigmata of hereditary syphilis, and in whom there were positive blood serum Wassermann reactions. The initial symptoms were vomiting, convulsions, stiffness of the neck, and flexure of the thighs on the abdomen. Kernig's sign was present in only one. Spirochetes were not found. There was rapid and permanent improvement under specific treatment. Vasiliu emphasizes the importance of investigating the antecedent and family history in all children exhibiting meningeal symptoms in which the cause can not definitely be determined.

#### REPORT OF CASE

An extremely emaciated male infant, twenty months old, of Italian parentage, was admitted to the wards of the Rochester Municipal Hospital 18 hours before

death. The parents admit syphilis, and the Wassermann reaction in each is four-plus. Another child of these parents, born two years before, lived six days.

The patient was born at term after a normal labor. At birth there were numerous palmar and plantar syphilodermata, which soon disappeared following the use of some "salve." Until two months before death, the parents say that he appeared to be in good health although undernourished. He was breast-fed for eight months, and after that received a miscellaneous diet. When eighteen months old, the parents first noticed a gradually increasing irritability, together with a slight opisthotonos; at first only occasionally, but with steadily decreasing intervals between attacks. A physician was consulted, who was acquainted with the specific history of the parents, and who prescribed mercurial inunctions.

When admitted to the hospital, the emaciation was extreme. The central incisor teeth were present and appeared normal; the skin free from sears or eruption. The body was in opisthotonos with general convulsions, affecting, particularly, the respiratory muscles, and causing partial asphyxia during the attacks. Temperature was 101.4°; pulse, 100; respirations, 36. The pupils were dilated, equal, and sluggishly responsive to light. The spinal fluid was slightly cloudy, under moderately increased pressure. A centrifuged specimen was negative for bacteria by ordinary staining and cultural methods. Smears prepared with India ink and with the Fontana stain showed numerous spirochetes. The blood serum Wassermann reaction was four-plus and there was complete fixation with .4 c.c. of spinal fluid. Necropsy was refused.

In the report of this case, I am indebted to Dr. Joseph Roby, Acting Health Officer of Rochester, N. Y.

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## HISTOGENESIS OF CEREBRAL HYPERTROPHIC PACHY-MENINGITIS AND ITS RELATION TO SYPHILIS

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THE name "pachymeningitis" was given by Virchow<sup>1</sup> in 1856 to a condition of chronic inflammation of the dura mater. The inflammation "leads to a formation of a fibrinous exudate" that organizes into a pseudomembrane which merging with the old surface causes some thickening. The new membrane is very rich in vessels and capillaries which rupture, the resulting hemorrhages becoming transformed into another vascular pseudomembrane. This in its turn ruptures causing a fresh hemorrhage and so forth. A vicious circle, as it were, thus forms, and it is hard to make out which is the primary factor, the new membranes formed by the hemorrhages, or the latter originating in the former. The hemorrhages are usually small, interlamellar, i. e., they take place *between the* membranes. Sometimes, however, they may be so extensive as to fill up the larger part of the subdural or subarachnoid space being often surrounded by or inclosed within a sac of connective tissue. Such hemorrhages have been named by Virchow hematoma duræ matris, and when enclosed within a sac they are also described as subarachnoid cysts.

Some authors accept a third variety, under the name of traumatic or meningeal hemorrhage, when accumulation of blood underneath the dura is the result of some trauma, surgical operation on the skull, hemorrhagic diathesis or penetration of an apoplectiform focus into the subdural space (Jores<sup>2</sup>).

While there is little doubt as to the origin of the blood in the last two varieties—hematoma and meningeal hemorrhages—which is ascribed (wrongly, probably,) to the rupture of the dura vessels, the question as to the origin of the pseudomembranes, their nature, histogenesis, is up to this time a subject of great controversy, and is by no means settled.

The majority of authors are inclined towards Virchow's theory

that the primary factor is a membrane formation, the hemorrhages being secondary, coming from the ruptured vessels of the new membrane.

This theory has been in vogue before Virchow's time and was defended by Bayle,<sup>3</sup> Baillie,<sup>4</sup> and Heschl.<sup>5</sup>

The opposite view was ably defended by Baillarger<sup>3</sup> and Huguenin,<sup>6</sup> namely, that the hemorrhages occur first, followed by a new membrane formation, as the result of the hemorrhages. Neither of these two theories seemed to be satisfactory to some investigators, and of late Jores<sup>2</sup> with his pupils, Laurant,<sup>7</sup> Van Vleuten,<sup>8</sup> promulgated a new theory. According to these authors, the inner layer of the dura which is normally very vascular becomes the starting place for excessive proliferation of capillaries which rupture and ultimately lead to a pseudomembrane formation.

Another theory, that of Barrat,<sup>9</sup> is that in hemorrhagic pachymeningitis vascular changes obtain in the form of intravascular fibrin formation that cause a thrombosis. The latter brings on a rupture of the vessels with hemorrhages, etc.

Of all these four theories the most popular one is that of Virchow which is also accepted of late by Melnikow-Razwedenkow,<sup>10</sup> and Marie, Roussy and La Roche<sup>11</sup>. According to any of these four theories a pachymeningitis is a morbid process of the dura itself, originating within this membrane, and is looked upon as an inflammatory process.

The study of the literature further reveals another striking feature, namely a total disregard of the etiologic factors that may be instrumental in the causation of this morbid condition, and lack of detailed studies of possible histologic changes in the piaarachnoid. This contention pertains to every type of pachymeningitis, be it a subdural hemorrhage, a subarachnoid cyst, or a so-called spontaneous pachymeningitis in which no large hemorrhages are present.

In the latter form, instead of subdural blood clots, enormous thickening of the membranes is found and it would be proper to call such cases *cerebral hypertrophic pachymeningitis* in analogy to hypertrophic *spinal* pachymeningitis.

This form of pachymeningitis is quite rare though it is referred to already by Virchow, Heubner,<sup>12</sup> Huguenin and others. In some monographs on nervous diseases it is spoken of as hyperplastic fibrous meningitis (Nonne, Forster), and sclerogummatous meningitis (Sézary). This type of pachymeningitis was not given the attention

it deserved, in contrast to the previous types mentioned which have been attracting the attention of investigators for the last hundred years or more. Yet the study of the histopathology of this type may and can clear up the real histogenesis of pachymeningitis in general, i. e., whether the primary, the essential process is an inflammation with a concomitant pseudomembrane formation, or hemorrhages.

My own studies of two cases of this type lead me to the conclusion that in hypertrophic type of pachymeningitis, or fibrous hyperplastic meningitis, the primary lesion is in the vessels, *that the sole cause of the lesion is syphilis, and that there is a simultaneous involvement of all the three membranes, including the brain tissue proper.*

The results are practically similar to those I arrived at from the histopathologic studies of the other types of pachymeningitis, the subdural hemorrhages, to be published in a separate contribution elsewhere.

CASE 1.—White man, 56 years old, entered the nervous service of Cook County Hospital, October 1st, 1917, with the history of epileptic fits. They started four months previously, up to which time he claimed having been well. He denied lues, gonorrhea, alcoholism or any other infectious disease. A complete and reliable history was hard to obtain, as the patient was very excitable, irrational, violent at times, disoriented as to time, place and persons.

There was complete loss of memory for recent events, but no aphasia, no paralysis, no signs of head injuries. The bony and muscular systems were well developed, general nutrition was good, the pupillary, skin and tendon reflexes normal. The appetite, bowels and urinary functions were also normal. The heart showed a slight apical murmur, the blood pressure was 132 systolic, 80 diastolic. The spinal fluid gave 60 cells (lymphocytes) per cubic millimeter. A Wassermann was not taken. During the following days there were repeated convulsions followed by stupor, a bilateral lobar pneumonia set in to which the patient succumbed nine days after his admittance.

The postmortem revealed "an internal hemorrhagic pachymeningitis, atrophy of the cerebral cortex, edema and hyperemia of the leptomeninges, right lobar pneumonia and pleurisy, syphilitic and senile sclerosis of the thoracic and abdominal portions of the aorta."

The dura upon further examination was found thickened all over the parietofrontal regions where it attained a  $\frac{1}{2}$  inch thickness. It could not be separated from the pia to which it was closely adhered,

and over the right parietal and temporal areas there were three thick separate membranes which became coalescent toward the motor region where they formed a scar tissue. The subdural and subarachnoid spaces were totally obliterated.

On close inspection, the thickened membranes showed about eight distinct pseudomembranes firmly attached to each other as well as to the dura. They could not be divided from each other without a sharp knife, and when cut apart each pseudomembrane appeared hard, cartilaginous and rusty looking. Each membrane was separately studied on frozen, celloidin and paraffin sections and stained with hematoxylin-eosin, Weigert's elastic stain, Van Gieson, scarlet red, toluidin blue and Alzheimer-Mann method (methyl blue-eosin).

Horizontal or surface sections of the dura itself, of its various layers, showed the normal array of its fibers intermingled with a great number of elastic fibers, and forming bundles crossing and intersecting each other. The nuclei of the fibers were very distinct, oval or spindle-like in shape, containing numerous small chromatin granules. The bundles were separated by interspaces and contained in some regions lacunæ which like the interspaces were usually free from any contents, as blood, though some interspaces especially in the inner layer of the dura showed the presence of hemorrhagic foci. Of other cells mastcells were very frequent, as well as so-called corpora arenacea.

The vessels of the dura were quite prominent, with their walls thickened, often homogeneous, i. e., a sharp distinction between the three layers could not always be made out. The intima in some cases exhibited large endothelial cells, and was as a rule proliferated almost totally occluding the vascular lumen. The adventitial layer contained an enormous amount of thickened and proliferated elastic fibers, while the elastic membrane frequently showed so-called "splitting" of its fibers. A very striking feature was so-called miliary gummata, which were in the form of larger or smaller foci of infiltration consisting principally of small lymphocytes and a few plasma cells near the vessels. Any other inflammatory phenomena, as fibrin fibers, perivascular cellular infiltrations, the presence of so-called rod cells ("Stäbchenzellen"), of fibroblasts were in the dura, in its various layers, totally lacking.

As a detailed description of each of the eight pseudomembranes would take up too much space I will merely give a brief outline of their histologic structure. In all of the pseudomembranes evidences

of old hemorrhages could be distinctly seen. They were in the form of pigment, blood cells and fibrin. Pigment was present in the form of granules and globules, scattered as free bodies, covering the interspaces and the collagen fibers of connective tissue, or gathered around the vessels, lacunæ and capillaries. More frequently was the pigment found enclosed within macrophages,—large oval or round while cells divided by numerous trabecula into vacuoles and containing a peripherally located, usually flattened nucleus. Pigment could also be found within fibroblasts, young connective tissue cells, spindle-like in shape with an oval nucleus, rich in chromatin. Not each membrane contained equal amount of pigment which was to be found in larger quantities in the younger membranes, nearer to the brain tissue. Fibrin was represented by very small thin films, mostly homogeneous in appearance, frequently eaten away or excavated at the edges. The excavations were usually packed with plasma cells, and by joining the neighboring excavated films formed a network. The films occasionally showed on their surface thin connective tissue fibers.

Blood elements were mostly in the form of modified lymphocytes—plasma cells, polyblasts, macrophages, and gitter cells. The plasma cells were especially numerous near the blood vessels, showed a rich cytoplasm with an excentrically located nucleus where the chromatin exhibited the distinct spoke-like arrangement. They occasionally contained 2-3-4 nuclei, and the latter frequently could be seen without any cytoplasm, forming dense foci. Some plasma cells were of unusually large size and often appeared in the form of previously mentioned fibroblasts. They were very numerous in every pseudomembrane, especially so in the older ones that were farther away from the pia. The macrophages, large vacuolated white cells, were always packed with pigment globules, while the gitter cells, reticular in structure with dislocated, usually flattened nucleus, were filled with lipid substances (on scarlet red specimens).

Aside from these four types of hematogenous elements—plasma cells, fibroblasts, macrophages and gitter cells—there were numerous polyblasts, i. e., modified lymphocytes, which play a tremendous role in the formation of new connective tissue.

All these cells were scattered among capillaries, vessels, and connective tissue fibers. The vessels, even the smallest, like the capillaries, possessed a well-developed adventitia, while the larger ones

showed a rich network of elastic fibers and a proliferated intima. Many vessels were densely surrounded by miliary gummata (Fig. 1).

The collagen fibers of connective tissue were present in each pseudomembrane, especially in the older ones near the dura, where they formed distinct bundles and meshes, and in each pseudomembrane the process of its formation from the above-mentioned blood cells—polyblasts, plasma cells—could be well followed up. The presence of miliary gummata, of proliferated intima, splitting of the elastic membrane indicates the syphilitic nature of their lesion, and it would be logical to assume that the vessels were the cause of the hemorrhages, were the source of the hematogenous elements instrumental in the upbuilding of the pseudomembranes. Any inflammatory phenomena, as perivascular infiltrations, etc., were, as in the dura, absent.

Still more striking are the pathologic findings in the piaarachnoid. These two membranes exhibited a tremendous distention, hyperemia, and wealth of pia meshes, their infiltration with various cells, mostly lymphocytes and plasma cells. The same vascular changes were present in the brain tissue itself which exhibited a great wealth of capillaries, always hyperemic and distended, but without any perivascular infiltrations. In other words, signs of inflammation as found in various forms of leptomeningitis, or in dementia paralytica, were in the pia and the brain tissue totally lacking.

The pathologic changes in this case can be summed up as miliary gummata and endarteritis, in short, as syphilitic meningoencephalitis.

Still more pronounced were these changes in the next case.

CASE 2.—Colored man, 26 years old, entered my service at the Cook County Hospital on July 5, 1916, complaining of severe headache, sore throat, chills, and fever. The headache started two months previously. It was very severe, depriving the patient of sleep, was not accompanied by vomiting, and was confined mostly to both temples. The sore throat was of three weeks' and the chills of one week's duration. The appetite and bowels were good.

*Previous History.*—Scarlet fever in childhood, gonorrhea three years and chancre six years before his entrance to the hospital.

*Examination.*—A well nourished colored male with normal bony and muscular systems, without any signs of paralysis, or deformities. There was a slight sensitiveness upon percussion of the frontoparietal region. Pupils were regular, equal, and normally reacted to light and in accommodation. The eye fundi also were normal. The skin and tendon reflexes, the sensibility, speech and mentality did not



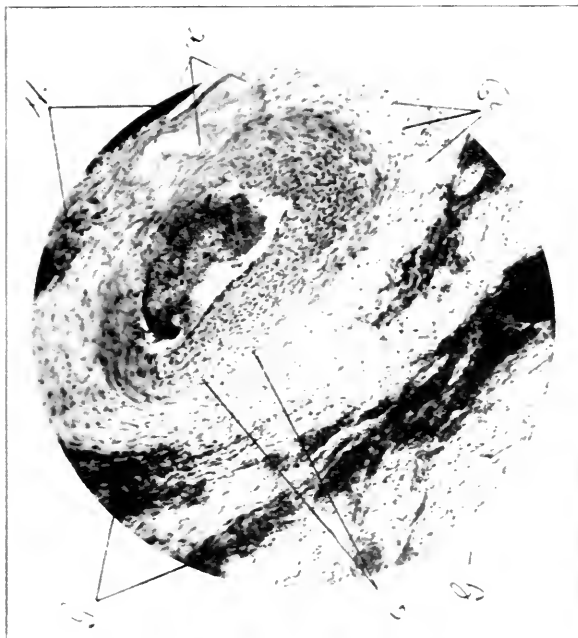


Fig. 1.—Dura from a case of syphilitic pachymeningitis. *D*, dura mater; *L*, lacunæ; *E*, elastic membrane; *G*, miliary gummata. Hematoxylin-eosin stain. Magnification 100 diameters.

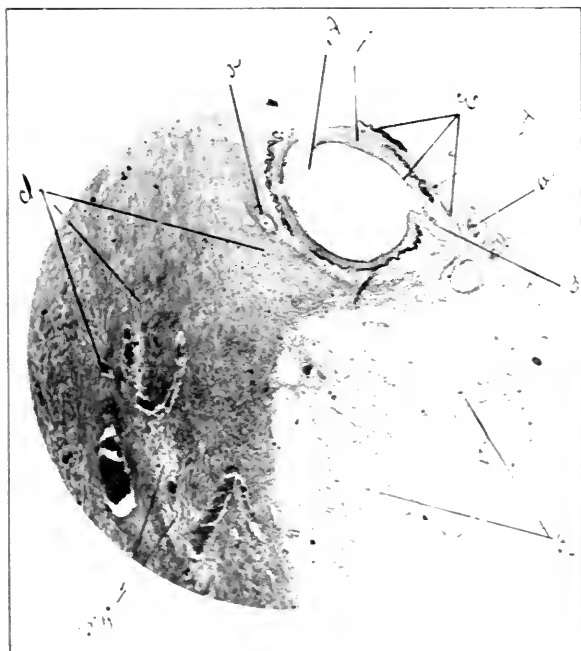


Fig. 2.—The pia and brain tissue in a case of syphilitic pachymeningitis. *Br*, brain; *P*, pia; *A*, artery; *E*, membrana elastica; *H*, hemorrhagic focus; *B*, horseshoe excavation of the intima. *G.C.*, Gitter cells. Elastica stain of Weigert (resorcin acid fuchsin). Magnification 36. (A hand lens will bring out the details better.)



show any abnormalities. The blood pressure was 125 systolic and 85 diastolic. A week later the patient showed apathy, disorientation, hallucinations of vision and hearing. He also exhibited great physical weakness, and complained of severe headache. There were during this time occasional twitchings in the face and limbs. From July 16 to July 24 he was feeling fairly good, when, i. e., on the 24th of July, convulsions set in with intervals of 5 minutes to an hour. Next day he had fifteen convulsions; on the 26th they were practically continuous, every 10 minutes with a temperature of  $104^{\circ}$  (rectal), the convulsions having continued the whole of the 28th of July when the patient died in status epilepticus. -

The convulsions usually started in the right arm, whence they were spreading to the rest of the body, accompanied by foaming at the mouth, urinary and rectal incontinence, complete general anesthesia, turning of the eyes and head to the right and elevation of temperature ( $103^{\circ}$ - $104^{\circ}$  per rectum).

The spinal fluid was under slightly increased pressure, clear, gave a strong positive Wassermann with 70 lymphocytes per cubic millimeter. The blood also showed a positive (slightly) Wassermann, and the urine was negative.

The postmortem examination revealed among other findings enormously thickened membranes, especially over the right frontoparietal region where the thickness was about three-quarters of an inch. The dura was closely adherent to the piaarachnoid with which it formed one solid parchment-like mass. The pia and the adjacent brain tissue exhibited a number of gummata. The subdural and the subarachnoid spaces were totally lacking, having been occupied by the pseudomembranes which, as in the previous case, formed several layers that could not be separated from each other without a very sharp knife.

Transverse sections were made through the entire thickened mass, as well as horizontal sections of each pseudomembrane, and stained with the same methods as in the previous case. To avoid repetitions I will illustrate the pathologic findings in this case by a few photomicrographs. Fig. 1 shows the dura at *D* with its nuclei (black dots) and the lacunal (*L*) which are free from blood or any other contents. The surface at *H* shows two hemorrhagic foci. The upper half of the picture is occupied in the center by a large artery partially filled with a thrombus. The walls of the artery are greatly infiltrated, especially the intima which is thickened, occupy-

ing the space between the elastic membrane (*E*) and the lumen. The elastic membrane is in the form of pale zig-zag line and does not always show very clearly with hematoxylin stain, but can be easily distinguished with the help of a hand lens. The large black masses covering the lower half of the picture are gummata consisting in this case of dense infiltration foci of small lymphocytes. In some of the gummata the foci of infiltration are so dense that they entirely cover up or occlude the vascular lumina. Any other cells, as plasma cells, giant cells, and regressive changes were absent. The pia changes are shown in Fig. 2. The pia appears greatly distended containing numerous dilated and pathologically changed vessels. At *A* an artery is seen with a double elastic membrane (*E*) and enormously proliferated intima (*I*) situated between the old and newly formed elastic membranes. At *B* the intima is excavated, horseshoe-like, and contains a thrombus. The splitting of the external elastic membrane is very marked. The muscular layer, following the elastic membrane appears homogeneous, containing a hemorrhagic focus, while the adventitia is proliferated. It clearly shows newly formed vessels within (arteries and veins-a). The pia on control specimens stained with toluidin blue shows various cells, mostly lymphocytes, fibroblasts, so-called rod cells ("Stäbchenzellen") and gutter cells forming here a large focus (G. C.).

The pia changes can also be followed up in Fig. 3 which exhibits a large number of distended and thrombosed vessels, mostly veins and an enormous infiltration of the pia. The brain tissue is covered with a great number of larger and smaller vessels, all of which are distended, filled with blood, and partly thrombosed. One gains an impression as if the brain tissue is turned into a network of vessels enclosing within their meshes the ganglion and the glia cells.

Some brain sections as shown in Fig. 4 exhibit nothing but vessels and miliary gummata, greatly resembling the infiltrated pia (*P*) from which the brain tissue can not be differentiated. The pia and the brain practically look alike, both consisting of proliferated vessels and miliary gummata. In other places the destruction of the brain tissue is less pronounced, the ganglion cells, the glia tissue being still in existence, but greatly changed. Thus, the ganglion cells with their processes exhibit various pathologic conditions described by Nissl and his pupils, ranging from common breaking up of the Nissl bodies, so-called chromatolysis, to their total disappearance when there are left but mere traces of a cell body usually invaded by glia

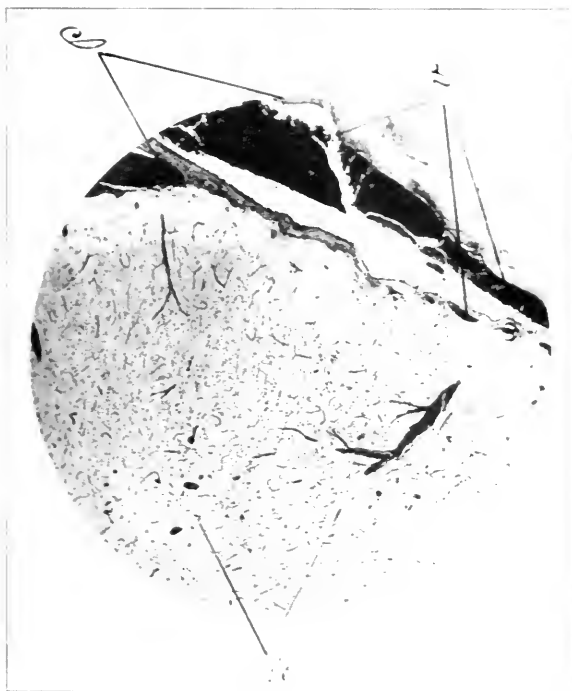


Fig. 3.—Pia and brain from the same case. *P.* pia; *V.* vein; *B.* brain tissue covered with numerous vessels and capillaries. The small black spots are glia cells. Alzheimer-Mann stain. Low power, magnification 24 diameters.

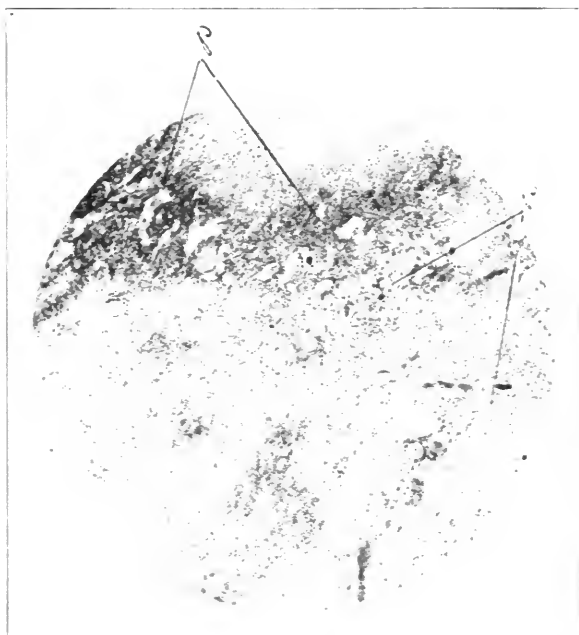


Fig. 4.—The pia and brain tissue in a case of syphilitic pachymeningitis. *P.* pia; *B.* brain tissue. Both tissues look alike and show numerous vessels and gummata. Hematoxylin-eosin stain. Low power, magnification 50 diameters.



cells (neuronophagia). The latter were greatly proliferated surrounding in increased numbers almost every ganglion cell, a condition known as satellitosis.

The parenchymatous changes very much resembled those found in general paresis, except the condition of the vessels which did not show the perivascular infiltrations with plasma cells and except the absence of so-called rod cells. The condition of the membrane and brain would justify the diagnosis in this case of syphilitic meningo-encephalitis.

The study of the pseudomembranes gave practically the same results as in the previous case. They showed as ready well developed membranes, exhibited an abundance of hemorrhages, of pigment globules, and of various cellular elements (lymphocytes, polyblasts, plasma cells, fibroblasts, macrophages and gitter cells). They also showed an enormous amount of miliary gummata and the presence of fat-like, so-called lipoid, substances. The latter as well as the above-mentioned cellular elements were totally absent in the dura, but present in the piaarachnoid. The question arises, Whence did such well-organized pseudomembranes come? Are they the result of an inflammatory state of the dura, i. e., a primary phenomenon, leading to hemorrhages, or are they formed from the various blood elements to be found in such an abundance in the piaarachnoid and in the pseudomembranes? To avoid extensive discussions I will merely point out the undisputable facts that in these two cases the morbid changes in the dura and piaarachnoid were frankly syphilitic in character, and much more pronounced in the piaarachnoid, than in the dura. Syphilitic changes of the cerebral membranes center practically around the vessels and gummata formation. The vascular changes, with or without formation of gummata, result in endarteritis, thrombosis, and ultimately in a rupture of the vessels with subsequent hemorrhages. The hemorrhages furnish the elements for formation of new membranes, just as they do in forming connective tissue membranes around an abscess, for instance.<sup>13</sup> It follows, that the pseudomembranes in both these cases must be looked upon as secondary to the vascular changes. There have been cases reported (Beck,<sup>14</sup> Le Count and Dewey,<sup>15</sup>) in which a syphilitic pachy or lepto-meningitis was confined to the stage of hemorrhages, though in Beck's case the dura was much thickened and covered with pseudomembranes which formed sacs filled with blood. Clear as the vascular changes were in

Beck's case, yet he considers them secondary to an inflammatory exudate supplied by the inflamed dura. However, the dura did not show in my cases any inflammatory exudate, in fact showed no inflammatory signs whatever, but exhibited like the piaarachnoid, and the latter to a much greater extent, vascular changes and the presence of various hematogenous elements supplied by the morbidly changed vessels. In other words, the vascular changes, especially in the piaarachnoid are the real, primary, factors instrumental in the formation and organization of the pseudomembranes. The pial ruptured vessels, namely, lead to hemorrhages which fill up the subarachnoid space where they organize into pseudomembranes and totally obliterate the space. The result is an obstruction to the circulation of the cerebrospinal fluid, an obstruction which may be partly responsible for the clinical symptoms. The piaarachnoid is supplied by the middle cerebral artery which as it is well known is the most vulnerable brain artery, while the dura, supplied by the middle meningeal artery, is as shown by Key and Retzius,<sup>61</sup> Michel,<sup>17</sup> Boehm,<sup>18</sup> and Langer<sup>19</sup> is much richer in blood supply than the pia, is well protected by the calvarium, has rich venous and arterial anastomoses, and is therefore in less danger of suffering from vascular disorders than the pia. The latter is supplied by the middle cerebral artery, which also nourishes the brain, its large basal ganglia, and when damaged by syphilis, old age, various infections and intoxications, some of its branches rupture, causing an apoplectic stroke in the form of a cerebral capsular hemorrhage. It would be logical to assume that the same factors, syphilis, old, age, etc., will cause a change and a rupture of the *pial* branches of this blood vessel, and a hemorrhage will obtain in the piaarachnoid with subsequent formation of a scar tissue in the subarachnoid space, that will cause marked thickening and adhesions of the membranes. That the etiologic factors above mentioned are instrumental in the causation of this lesion is evidenced by statements of older authors that pachymeningitis most frequently occurs in paralytic dementia which is at the present universally recognized to be syphilogenous disease. Yet Huguenin<sup>6</sup> in his classical treatise on disease of the cerebral membranes, in speaking of the etiology of internal pachymeningitis says: "Finally many cases exist where syphilis was supposed to be the original disease; the connection is not clear; certainly no one will be disposed to refer the affection to Heubner's disease of the cerebral vessels (page 403.)"



Needless to say that such an assertion is absolutely untenable, as the type of pachymeningitis under discussion is exclusively due to syphilis, to the syphilitic lesions of the cerebral vessels. I wish again to point out the fact that of the cerebral vessels, the dural, or the middle meningeal artery, hardly plays any role in the causation of pachymeningitis as Kremiansky<sup>20</sup> tried to prove pathologically and experimentally, and that the principal seat of the morbid phenomena are the *pial* vessels. The name "pachymeningitis interna," is therefore a misnomer, and the terms "fibrous hyperplastic meningitis" as used by Nonne,<sup>21</sup> Forster,<sup>22</sup> or that of sclerogummatous meningitis (Sézary)<sup>23</sup> should be used instead. Such types of meningitis can be looked upon as a distinct group where the syphilitic process involves the meninges not at the base, but on the convexity.

Such exclusive localization with the simultaneous involvement of all the membranes is by no means frequent. Thus Le Count and Dewey,<sup>15</sup> record 55 cases of syphilitic leptomeningitis with careful macro- and microscopic reports of each individual case, and only in two (Cases 11 and 55) was the dura found thickened, while in the rest of the cases the piaarachnoid alone was involved.

Other, less extensive and elaborate, statistics also show the relative rarity of this type of meningitis, its rather unexpected or accidental detection on the postmortem table, as clinically so far it remains undiagnosed. Yet, the clinical value of the hypertrophic or hyperplastic type of meningitis is tremendous as the prognosis is very bad which is understood in view of the profound and various changes described above.

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## SYPHILIS OF THE LARYNX

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**S**YPHILIS of the larynx is not an infrequent disease, when we make a comparison of the number of cases that we see in a long interval of observation with malignant and nonmalignant neoplasms and ulcers of the larynx.

Syphilis of the larynx may be complicated or uncomplicated. The most frequent complication probably found is tuberculosis and syphilis combined.

A classification of syphilis as seen by me and for discussion follows:

1. Mucous patch.
2. Thickening of the vocal cords or hyperplasia.
3. Paralysis of one or both vocal cords.
4. Paresis (variable week by week).
5. Gummata.
6. Ulceration.
7. Cicatricial changes in the vocal cords.
8. Involvement of contiguous parts to the vocal cords.

The cause of syphilis is primary infection of the blood vessels and lymphatics of the mucous layer of the skin or mucous membranes with *treponema pallidum*, either by direct contact or accidental inoculation from one individual to another by use of dirty instruments or accidental puncture of the skin by a needle in operating.

Syphilis of the larynx may be acquired or inherited. It may be primary, secondary, or tertiary.

The location of the larynx is such as to prevent infection by personal contact. The cases that have been reported by Bosworth, Professor E. J. Moure of France, Sir Morele Mackenzie and others were carried probably by unclean instruments from the mouth of a patient with a primary chancre to an innocent victim, while in the act of making a local application to the larynx.

In an individual with a primary sore in the mouth, the *Treponema pallidum* may be found swimming in the lymph spaces in the act of talking or kissing, directly spray the organisms into the mouth of another and thence to the broken surface of the larynx. The spirochetes are a motile microorganism as shown by dark illumination in a microscopical examination. It has great vitality and can live in a medium where many other organisms would soon lose their vitality. The spirilla of Vincent, which remains in the mouth of infected individuals for a year or more, show the wonderful vitality of this species, which has come to occupy a place alongside the *Spirochete pallida*.

Thickening of the vocal cords gives rise to periodical attacks of hoarseness, or the so-called raucous voice, especially after using the voice. Examination of the cords at such a time gives a pinkish discoloration and dilated and tortuous blood vessels. This condition is observed especially in the tertiary stage and without any symptoms of paralysis. The Wassermann test is at this time usually positive and the patient has been neglecting his treatment for a long time. He probably smokes too much and may be a periodical drinker. Otherwise the patient may appear the picture of perfect health. Hoarseness drives him to his doctor and thus he escapes ulceration and cicatricial changes.

Paralysis is more often confined to the abductor muscle of one side. The cricoarytenoideus lateralis is the especial abductor muscle and is supplied by a branch of the recurrent nerve from the vagus. Paralysis of one side may be from a local inflammation in the muscle or a peripheral neuritis.<sup>1</sup> Observation may show at this time one cord faulty in movement or standing fixed in a median line. Cases of complete paralysis of one side may without discovery have an abductor paralysis come on suddenly and die very quickly from suffocation. Examination of a patient in great distress may disclose a complete paralysis and a history of an inability to get his breath. The acute side may suddenly turn out and restoration of function occur in a short time.

I have seen two cases die from sudden spasm of an abductor muscle of an apparent well side and an abductor paralysis of the opposite side that had existed for a period of time. Death came so suddenly that a tracheotomy was out of the question. A patient with a history of spasms of breathing, or difficult inspiration, voice

crowding in character and rapid pulse, should be operated at once, and medicinal treatment instituted afterwards. The recovery of such a patient is usually rapid and the tracheotomy tube may be removed as soon as the cords become active again. Paralysis of this character may come on the newborn and suffocation follow, without any postmortem findings. Long after birth, if the tertiary lesion is present, a spasm of the larynx may come on without any history of subsequent symptoms of the disease. For reference see Doctor Campbell's article<sup>2</sup>. He makes a true statement that in establishing a diagnosis of hereditary syphilis, "there are three points known as the triad of syphilis, which have long been looked upon as of the greatest value. These are namely, Hutchinson's teeth, interstitial keratitis and auditory deafness" and I might add persistent enlargements of the deep cervical lymphatics of the neck.

Campbell's article dates many years back, but to quote him further and call attention to those versed in the use of the ophthalmoscope, to the following,<sup>3</sup> "Edmond Fournier and some other French physicians lay great stress on the findings in the fundus of the eyes as an aid in the diagnosis of hereditary syphilis. In one case he described chorioretinal plaques in both eyes. In another case the remains of an old papillitis were seen. Vascular changes and alteration of pigment, which oculist Antonelli stated could be the stigmata of hereditary syphilis, were observed in one eye and in the other, there was a rudimentary optic neuritis, a diffuse retinitis of several months' standing, manifesting itself as severe foci of exudation in the cerebral region, by a suffusion that was quite intense, and by multiple separation of the retina in the temporal and upper sections of the fundus. "Unlike early acquired syphilis, in hereditary syphilis we never have any scaly or small eruption of the skin."

It requires very little inflammation of the recurrent laryngeal or pressure to produce a paresis or a paralysis. The great number of cases of paralysis in the tactile sense are recognized by pressure in the branchial plexus. A condition of paresis or paralysis responds quickly to medication. Muscles other than the abductor could be mentioned, but our reference to the most important and fatal form of disease of the larynx is sufficient to direct the reader's attention to the other like complications, especially aphonia.

Gumma of the larynx is far more frequent than hyperplasia or paralysis. A gumma usually breaks down and leads to a chronic

suppuration, involving the mucosa, perichondrium and cartilage of the laryngeal box, and is sometimes, in the absence of a positive Wassermann test, mistaken for a tuberculosis. Frequently, however, gummata and laryngeal tuberculosis are complicated and the case takes on a peculiar process of destruction and physical changes. These cases are very intractable and hard to reach. The combinations advance rapidly and many times the parts under observation may be practically destroyed. The patients suffer from radiating pain in the ears, difficulty of swallowing, or in taking solid or liquid food, accumulation of mucus, inability to sleep, progressive emaciation and death. Examination may show grayish red, or grayish yellow with a strongly defined outline. This may for a time cause little distress. Gummata may at the same time be in the thyroid or small bronchi (Davis)<sup>4</sup>. Gummata occur below the vocal cord and involve the aryoid and cartilaginous regions of the trachea and produce cicatricial changes and death. Whenever the glands of the neck persistently enlarge and the tonsils have been enucleated, one should think of inherited syphilis or acquired syphilis. Many cases have a slight taint of inherited syphilis, and never develop a characteristic lesion, but respond to the iodides very quickly. I have seen this occur in apparently healthy babies. In one case of a baby about one year old, the posterior neck muscle began to pull the neck backwards. Administration of iodides gave almost instant relief. There were no other symptoms of disease. A gumma may involve the arytenoids, vocal cords or epiglottis. The swelling may come on so rapidly as to necessitate a tracheotomy. Again, as in paralysis of the cord, a tracheotomy should be advocated and heavy antisyphilitic treatment begun. Iodide of potassium in large doses is indicated in uncomplicated cases of gummata, but with a complication of tubercle bacilli the results are usually bad. Iodides should be pushed to the full constitutional effect, that is, in nasal hydrorrhea. It should not be continued too long afterwards on account of its tendency to produce a lessening of the red corpuscles and consequent loss of flesh.

In the diagnosis of gummata of the larynx, one must consider the history of the case, the Wassermann reaction, and the possibility of a neoplasm. In a gumma and a neoplasm, the symptoms of hoarseness are quite the same. Slight hemorrhage may accompany either condition and emaciation and slight rise of temperature may also occur. The diagnosis is by exclusion. Absence of a history of pri-

mary lesion or skin eruption have no weight as evidence that the growth in the larynx is not a gumma. Under antisyphilitic treatments, deformities or cicatricial changes are to be anticipated.

Ulceration may be slow or rapid in its progress; time is not taken into consideration by this disease. Beck<sup>5</sup> says, "in the perichondrite form of laryngeal syphilis in the arytenoid that is most frequently involved and is a late secondary process." There is usually a median placement of the cord and the arytenoid is fixed and in the breaking down process or abscess formation the arytenoid has a tendency to bear forward and inward and since the aryepiglottidean fold is usually very much swollen or edematous, one can expect considerable difficulty in breathing. In one case of suppuration of the arytenoid process, the broken cartilage was expelled by coughing. The cricoid is next most frequently involved.

Beck<sup>5</sup> also mentions a condition which is frequently observed, that is a general narrowing of the larynx from cicatricial tissue, probably originating submucously. This latter condition readily responds to salvarsan.

Cicatricial changes in the vocal cords, arytenoids and trachea are not infrequently found. It resembles, when present, the deep cicatricial changes one sees in the nasopharynx in many cases following diphtheria.

Many physicians prescribe kali iodide in all cases of local conditions and without a Wassermann test. Physicians even today, when the percentage of people who have syphilis is about 20 per cent, will not inquire of the patient the possibility of such an affection, on account of wounding the patient's vanity.

After ulceration and destruction of the epithelium of the vocal cord, it is a very easy proposition for the cords to close with adhesive bands. Such a case is difficult to heal, for there is a greater tendency of a cicatrix from irritation of contiguous tissue to extend by encroachment by submucous thickening and obstinately reforms after the operation. This condition has been impressed upon me by a case of inflammation of the cords and subsequent adhesions due to, acid preparations reaching the larynx. A laryngotomy and an up and down laryngeal tube worn for a long time may break the attachments of the cords. Cicatrices in any part of the nasopharynx, larynx and esophagus defy treatment. Suspension enables the operator to view the adhesive bands very easily and to dilate the glottis, but it is

especially difficult in the very young. Stricture in the bronchi may be dilated by long rubber bougies with the aid of a bronchial cape. (See the work of Killian).

Affections of contiguous parts to the larynx are not, according to the literature, a frequent condition, and I refer the reader to a wonderful compilation on the subject by Davis.<sup>6</sup> Involvement of the thyroid gland in the tertiary stage usually give a history that suggests syphilis, but is a struma syphilitica.

The local symptoms are as described by Davis: "(1) Cases in which the swelling is hard and more or less painful, and (2) those cases in which the swelling is more or less soft and giving the patient no distress." From personal observation I have never seen a gumma of the thyroid gland. Up to the time of Davis' article in 1900, twenty cases had been described in the literature. Probably a gumma is primarily in the cartilage and submucosa of the larynx and extends by continuity of tissue and lymphatics to the thyroid gland.

The best results from salvarsan are in some cases from weekly injections and in others biweekly and in half the original dose. There should be no distinct and toxic effect in the use of salvarsan, except a sense of disagreeable odor, that comes with the first entrance of the salvarsan into the blood stream. The flushing of the face is to be expected. Large doses frequently produce severe headache, sometimes nausea, vomiting, and watery stools. Often there will be severe irritation and pain along the spine. This may last eight or ten hours and sometimes cause death.

As to the number of injections of salvarsan, they should be carried to the point of toleration and then stopped; this is, irritation of the skin and intestinal disturbance, which lasts sometimes for a week or more. One or two injections of salvarsan are of no lasting value except in the case of a mucous patch. In the ordinary cases of tertiary syphilis, 15 to 20 injections are necessary. Anaphylaxis may be expected, if the injections are stopped for many weeks and then begun again. Calomel ointment, 30 per cent, and kali iodide in small doses should be persisted in until all symptoms are relieved and pass away. Frequently during the interval of rest the Wassermann test is valuable, the iodides and mercury are in physiological action, the physician may be deceived by a negative Wassermann and the patient neglect his duty to be constantly under the care of his consultant. In any lesion of the larynx there is probably no danger



of what is known as the Herxheimer reaction. Many years ago, when salvarsan was first introduced, there was a theory that the auditory nerve or the cochlear branch was liable to injury, but this theory has been discarded a long time. Mercury has been in some form, preferably by inunction, the *sine qua non* of therapy as a curative agent. Kali iodide will dissolve gummata and throw the spirochetes loose and the salvarsan into an inanimate substance. Kali iodide interferes with the red corpuscles of the blood and will have a tendency to cause anemia. Mercury from the first history of syphilis has been the recognized treatment.

Baths and massage are to be recommended at intervals. Turkish baths are not indicated in any affection of the upper and lower air passages or even in health. Dry heat is the best thing to use in producing a free sweating. Sunlight and rest are most important. For the prevention of anemia, iron albumate and Blaud's pills are indicated after the kali iodide has been discontinued.

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## THE DIFFERENTIAL COUNT IN SYPHILIS

### A PRELIMINARY NOTE

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ALTHOUGH the differential count is seldom if ever employed to establish the diagnosis of syphilis, under conditions it may be of great assistance. It is known that in syphilis the number of lymphocytes is increased, but as such condition exists in a number of other diseases it is obvious that a lymphocytosis without clinical evidence or history is of little value for diagnostic purposes. If there is clinical evidence or a history of syphilis, the existing increase in lymphocytes may confirm the diagnosis of syphilis even when the blood Wassermann test presents a negative reaction, provided, that other conditions, usually accompanied by lymphocytosis, are absent.

In a number of cases the Wassermann reaction is negative with the blood of women who are married to men with a history of lues. Women, whose husbands were known to be luetic when tested after recent miscarriages frequently presented a negative Wassermann reaction. We did not consider the negative Wassermann reaction sufficient to disprove the evidence of syphilis in such cases, and resorted to the differential count, only to find a high percentage of either small or large lymphocytes—or both—present in almost every case.

1. \*Mrs. W. B. presents a negative Wassermann while the differential count is as follows:

Polymorphonuclears,	39%	Türk irritation c.,	1%
Large mononuclears,	1%	Basophiles,	2%
Large lymphocytes,	12%	Transicionales,	1%
Small lymphocytes,	44%		

The blood of the husband of this patient presented a picture as follows:

Polymorphonuclears,	57%	Small lymphocytes,	32%
Large lymphocytes,	9%	Transicionales,	2%

The Wassermann test was said to be strongly positive.

2. Mrs. R. W. presents a negative Wassermann. The blood picture is as follows:

Polymorphonuclears,	51.5%
Large lymphocytes,	3%
Small lymphocytes,	42%
Eosinophiles,	0.5%
Transicionales,	3%

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\*Altogether sixty cases were observed.

The husband presents a 100% positive spinal fluid Wassermann, an 80% positive blood Wassermann with a cholesterol reinforced antigen, and his differential count shows values as follows:

Polymorphonuclears,	57%	Small lymphocytes,	37%
Large mononuclears,	1%	Eosinophiles,	2%
Large lymphocytes,	1%	Transitionales,	2%

Such (lymphocytoses) were the results in untreated cases of syphilis in both men and women. We found moreover that the blood picture changed to normal under the influence of antisyphilitic treatment.

At the present time the findings lead us to believe that an increase of the large lymphocytes is primarily noticeable in the earliest stage of the disease. This condition is accompanied by a slight increase of eosinophiles. If treatment is begun immediately the changes in the blood picture become normal but very slowly.

3. Patient J. Primary sore appeared three weeks after exposure. *Treponema pallidum* demonstrated three days after appearance of sore. Differential count at that time was as follows:

Polymorphonuclears,	60.5%	Small lymphocytes,	9%
Large mononuclears,	2%	Eosinophiles,	6.5%
Large lymphocytes,	15.5%	Transitionales,	6.5%

Arsenobenzol (0.6 gram) was administered and when the treatment was repeated three weeks later, the blood presented the following:

Polymorphonuclears,	61.4%	Small lymphocytes,	30%
Large mononuclears,	0.4%	Eosinophiles,	4.4%
Large lymphocytes,	12.6%	Transitionales,	1.2%

The next injection of 0.6 gm. arsenobenzol was administered seven days later when the count was as follows:

Polymorphonuclears,	59%	Small lymphocytes,	19%
Large mononuclears,	4%	Eosinophiles,	3%
Large lymphocytes,	12%	Transitionales,	3%

Two weeks after the initial sore makes its appearance the small lymphocytes begin to increase, and at the time the Wassermann reaction becomes positive the amount of small lymphocytes is distinctly increased.

Patient Mrs. C., headaches three weeks after wedding day. Rashes one month after wedding day. Blood Wassermann 100 per cent positive. Differential count:

Polymorphonuclears,	54%	Small lymphocytes,	31.5%
Large mononuclears,	1%	Türk irritation c.,	0.25%
Large lymphocytes,	6%	Transitionales,	2%

Arsenobenzol treatment presents an increase in polymorphonuclears in cases where the Wassermann reaction is positive when treatment is begun. At first the large lymphocytes also increase, and the small ones decrease in number. The count is almost normal after the fourth injection of arsenobenzol. The number of polymorphonuclears varies between 69 and 75 per cent.

All of our blood specimens were obtained from patients who received their first four arsenobenzol treatments at intervals of from 8 to 15 days. We have had no experience with the blood changes that follow the more vigorous treatment.

4. Patient B., infected thirty years previously. Wassermann 100 per cent positive. Differential count:

Polymorphonuclears,	51%	Small lymphocytes,	46%
Large lymphocytes,	1%	Eosinophiles,	2%

Two weeks after the administration of 0.6 gm. arsenobenzol the count was as follows:

Polymorphonuclears,	48%	Small lymphocytes,	30%
Large mononuclears,	1%	Eosinophiles,	9%
Large lymphocytes,	.5%	Basophiles,	3%
Türk irritation,	1%	Transitionales,	3%

Ten days after the administration of the second dose of 0.6 gm. arsenobenzol the count presented following changes:

Polymorphonuclears,	60%	Transitionales,	5%
Large lymphocytes,	17%	Eosinophiles,	5%
Small lymphocytes,	13%		

Eleven days after the third injection of 0.6 gm. of arsenobenzol the count presented the following values:

Polymorphonuclears,	69%	Large mononuclears,	1%
Large lymphocytes,	9%	Eosinophiles,	2%
Small lymphocytes,	18%	Transitionales,	1%

5. Patient O. B. B. presents the following blood picture two weeks after the fourth injection of 0.6 gm. arsenobenzol:

Polymorphonuclears,	70%	Myelocytes,	1%
Large mononuclears,	0.5%	Eosinophiles,	5%
Large lymphocytes,	15%	Transitionales,	1%
Small lymphocytes,	12%		

Two weeks after the fifth injection the blood shows a picture as follows:

Polymorphonuclears,	78%	Small lymphocytes,	4%
Large mononuclears,	4%	Eosinophiles,	1%
Large lymphocytes,	10%	Transitionales,	3%

This patient received his first arsphenamine treatment six months after the appearance of primary sore.

In some instances the blood changes are slower.

6. Patient M. N., infected three years previously. Received three injections of salvarsan and three injections of arsenobenzol. The last three were administered within four months. At that time the blood count was as follows:

Polymorphonuclears,	43.5%	Small lymphocytes,	41.5%
Large mononuclears,	2.5%	Transitionales,	2%
Large lymphocytes,	10.5%	Türk irritation,	0.5%

Three weeks after the seventh injection of arsenobenzol the count was as presented here:

Polymorphonuclears,	45%	Small lymphocytes,	41%
Large mononuclears,	2%	Eosinophiles,	2%
Large lymphocytes,	9%	Transitionales,	1%

We have seen one case, recently infected, that obtained the mercury before the arsenobenzol treatment.

The patient was a federal prisoner presenting an intraurethral chancre and a mild eruption. When blood was taken for the Wassermann test, the reaction was 100 per cent positive. The patient received 12 mercurettes and one quarter of one pound of Ung. Hydrargyri ciner. U. S. P. Two weeks after the last rub the blood picture was as follows:

Polymorphonuclears,	70%	Eosinophiles,	0.2%
Large mononuclears,	1%	Transicionales,	3.5%
Large lymphocytes,	5%	Myelocytes,	0.3%
Small lymphocytes,	20%		

At this time, 0.6 gm. arsenobenzol was administered. Two weeks later the blood presented the following count:

Polymorphonuclears,	73.5%	Small lymphocytes,	8.5%
Large mononuclears,	0.5%	Eosinophiles,	0.5%
Large lymphocytes,	12%	Transicionales,	0.5%

Patients who receive intensive antisiphilitic treatment for a considerable period, and who constantly present a negative blood Wassermann reaction usually exhibit a persistent increase in the lymphocyte count of the large cell type.

7. Patient G. received last treatment three and one-half years previously. Wassermann reaction negative at present. Differential count:

Polymorphonuclears,	51.5%	Myelocytes,	0.5%
Large lymphocytes,	21%	Transicionales,	3%
Small lymphocytes,	16.5%	Eosinophiles,	8%

One is compelled to appreciate the value of the differential count, with a finding as presented in the following case:

8. Patient Sch. contracted lues 21 years ago. He received thirteen injections of the Ellis-Swift type during the years 1915-1916, followed by numerous mercury rubs. Spinal drainage was resorted to several times. The blood Wassermann reaction was constantly negative for the last two years.

The differential count at present is as follows:

Polymorphonuclears,	60.5%	Small lymphocytes,	21.5%
Large mononuclears,	1%	Transicionales,	2.5%
Large lymphocytes,	14.5%		

The spinal fluid Wassermann is strongly positive.

The technic of the Wassermann test adopted by us is the one described by Wehrbein (*Northwest Medicine*, March 1918, Seattle) together with the original one of Wassermann and the modification of Noguchi. The Wehrbein technic is very accurate and superior to most others.

We are continuing our observations in regard to the value of the differential count, and hope to furnish more exact conclusions. We are, however, certain that our counts dispute the sufficiency of a

negative Wassermann test one year from the date of the last treatment, as a favorable evidence. The negative blood and spinal fluid findings must be accompanied by a persistently normal blood count.

The administration of one injection of arsphenamine alters the differential count very little, and no matter how negative the Wassermann reaction is, we would say that so long as the blood picture does not return to the normal and remain so, the patient is not cured.

# SERUM DIAGNOSIS OF SYPHILIS AND GONORRHEA EMPLOYING HUMAN COMPLEMENT

WITH SPECIAL REFERENCE TO THE NOGUCHI HOMOHEMOLYTIC, HECHT, AND HECHT-GRADWOHL REACTIONS

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TWO years ago a series of investigations were undertaken in these laboratories upon the problem of the standardization of the Wassermann reaction<sup>1</sup> with the object of studying complement fixation in syphilis from many angles and with the hope that the work would result in the evolvement of a standardized technic built upon the basis of actual experiment and comparative studies with different methods. These investigations have included a study of methods tending to simplify the technic as that of Emery,<sup>2</sup> who uses the patient's serum in a fresh active state for both complement and antibody and completes the hemolytic system with antihumanamboceptor and human cells; of Butler and Landon,<sup>3</sup> who substitute human for guinea pig serum complement in the regular Noguchi test; of Health,<sup>4</sup> who uses human complement in an antisheep system, and of Hecht<sup>5</sup> and Gradwohl's modification,<sup>6</sup> employing the natural antisheep hemolysin in addition to the complement of the serum of each patient. All of these methods sought to avoid the use of guinea pigs and with the exception of the last two, to employ human cells with antihumanamboceptor and thereby simplify and increase the delicacy of the technic and render the test possible and available under adverse conditions. Recently Noguchi<sup>7</sup> has described a new test embodying the use of each person's complement, which he has found reliable and particularly serviceable for the serum diagnosis of syphilis under war conditions owing to a growing scarcity of guinea pigs and the necessity for economy in labor, expense, and time. This technic has been criticized by Seelman<sup>8</sup> and as my work was conducted with a modification of Emery's technic quite similar

to that devised by Noguchi, I have considered advisable the publication at this time of a brief account of the results of our studies, since the subject is of particular importance under present conditions.

#### TECHNIC OF THE NOGUCHI HOMOHEMOLYTIC COMPLEMENT TEST

My results with Emery's technic have been poor inasmuch as the quantities of various reagents employed by him are very small and rather indifferently titrated; furthermore his tests as recently described, employ an alcoholic extract of heart muscle reenforced with cholesterin as antigen and this extract has yielded a high percentage of pseudo or falsely positive reaction when used with active serum. Cholesterinized antigens have proved in my experience, quite delicate, reliable and highly satisfactory in the Wassermann reaction employing heated serum, but with active serum plain alcoholic extracts of syphilitic liver or normal heart muscle and particularly such extracts reenforced with cholesterin, are prone to yield falsely positive results. This has been found true in the original Noguchi test employing unheated human serum and guinea pig complement as emphasized by Noguchi himself several years ago and designated by him as "proteotropic reactions" and ascribed to the presence of proteins in the extracts responsible for the nonspecific fixation of complement, and is particularly emphasized in tests employing the complement of the patient's own serum as I have found with the Hecht-Gradwohl test,<sup>9</sup> because human complement is apparently more susceptible to proteotropic fixation than guinea pig complement. For this reason, I am firmly convinced that the best antigen to employ in all tests which utilize the complement of the patient's own serum, is the acetone-insoluble lipid extract of Noguchi; furthermore as these extracts ordinarily prepared may still yield a low percentage of pseudo or proteotropic reactions with active serum it is now my custom to purify them by re-dissolving the acetone insoluble residue in pure ether and reprecipitating with pure acetone, before preparing a 3 per cent solution in pure methyl alcohol.\* Butler and Landon, who use human instead of guinea pig complement in the regular Noguchi test, employ an extract of acetone-insoluble lipoids as antigen; Noguchi also employs this antigen in his new

\*Recently Noguchi (personal communication) has stated that by carefully decanting the clear, ether-soluble portion after letting the insoluble particles settle to the bottom by sedimentation overnight or longer in order to painstakingly remove the insoluble particles, refractionation is unnecessary.



technic and all of the work reported in this communication was conducted with several of these antigens after preliminary titrations.

Since human complement appears to be more susceptible to the anticomplementary action of antigen than guinea pig complement, I determine the anticomplementary and antigenic units of an extract with human instead of guinea pig complement when the antigen is to be employed in tests utilizing the complement of the patient's serum as in the Noguchi homohemolytic and Hecht or Hecht-Gradwohl tests; Emery likewise uses human complement for these titrations while Noguchi apparently titrates with guinea pig serum complement. In Table I are shown the results of titrations with two antigens of acetone-insoluble lipoids of beef heart; in the anticomplementary titrations the mixed serum of two normal persons was used in dose of 0.1 c.c. as complement, while in the antigenic titrations 0.1 c.c. of the mixed serum of three syphilitic persons furnished both the complement and syphilis antibody. The antigens were anticomplementary in dose of 0.4 and 0.3 c.c. of 1:10 dilutions, respectively, but with guinea pig complement in dose of 0.1 c.c. the anticomplementary units were 0.8 and 0.6 c.c., respectively; the antigenic units were 0.2 and 0.1 c.c. of 1:100 dilutions respectively, while in titrations employing 0.1 c.c. of active syphilitic serum and 0.1 c.c. of guinea pig serum complement, the units were 0.25 and 0.2 c.c. of 1:100 dilutions respectively. In conducting the main tests employing the patient's own complement, I used each extract in dose corresponding to five antigenic units and these amounts were always less than the doses indicated by titrations with guinea

TABLE I  
ANTIGEN TITRATIONS EMPLOYING HUMAN COMPLEMENT

ANTIGEN	ANTICOMPLEMENTARY TITRATION (1:10)					ANTIGENIC TITRATION (1:100)				
	0.1 c.c.	0.2 c.c.	0.3 c.c.	0.4 c.c.	0.5 c.c.	0.05 c.c.	0.08 c.c.	0.1 c.c.	0.15 c.c.	0.2 c.c.
Acetone-insol- uble lipoids No. S	H*	H	H	S.I.H.	M.I.H.	++	++	++	+++	+++
Acetone-insol- uble lipoids No. A	H	H	S.I.H.	M.I.H.	I.H.	++	++	+++	+++	+++

\*H = complete hemolysis; S.I.H. = slight inhibition of hemolysis; M.I.H. = marked inhibition of hemolysis; I.H. = complete inhibition of hemolysis.

\*\*\* = complete fixation of complement; ++ = 75 per cent inhibition of hemolysis; ++ = 50 per cent inhibition; + = 25 per cent inhibition.

pig complement; while it is advisable to use a sufficient amount of antigen, I believe on the basis of comparative tests, that it is not advisable to use more than the amount actually needed in order to reduce the percentage of pseudo reactions, and five antigenic units as determined in a titration employing the serum of a syphilitic for both complement and antibody, appears to be sufficient in the conduct of the main tests.

Probably the chief difficulty in conducting these tests was experienced with the antihuman hemolysin. I have generally experienced considerable difficulty in preparing a sufficiently powerful hemolytic serum in order to avoid the action of hemagglutinin; Noguchi regards a serum as satisfactory which produces complete hemolysis of 1 c.c. of 1 per cent human corpuscle suspension in a dose of 0.01 c.c. or less in the presence of 0.1 c.c. of fresh human complement within from twenty to thirty minutes at 37° C. in a water-bath; usually my hemolysins have been stronger yielding hemolysis of the same amount of cells (0.1 c.c. of a 10 per cent suspension) in the presence of 0.1 c.c. undiluted human complement serum, in dose of 0.1 c.c. of 1:20 or 1:30 dilutions (corresponding to 0.005 or 0.003 c.c. of serum), but even with these hemolysins, hemagglutination was usually a troublesome phenomenon and frequently interfered with hemolysis in the controls and main tests. In this connection I may state that the slower intraperitoneal route for immunizing rabbits with human cells has generally yielded better results than the intravenous route and serum dried on filter paper as originally devised by Noguchi, yields uniformly better results than serum preserved with phenol or glycerin and diluted with saline solution, inasmuch as hemagglutination is less evident, suggesting a deterioration of agglutinin during the process of drying the serum in paper.

The amboceptor papers cut into strips 5 mm. in width were titrated in increasing lengths with 0.1 c.c. of fresh undiluted human serum complement,\* 1 c.c. of 1 per cent suspension of washed human cells and water-bath incubation for half an hour. The results of titrations with the same paper and thirty-six different sera have shown that the complement activity of human serum varies but is

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\*In this connection mention may also be made of a phenomenon which I have observed on several occasions, namely, sera secured by breaking up coagulated blood within five or ten minutes after bleeding and centrifuging, may contain very small amounts of hemolytic complement, whereas if secured several hours after collection, usual hemolytic activity is observed.

found sufficiently uniform to enable one to select a unit on the basis of an average. In Table II I have placed the results of six of these titrations as examples of the degree of variation observed with one amboceptor and also to show that measures of paper in considerable excess of the unit may interfere with hemolysis, due presumably, to agglutination of erythrocytes which is usually detected by direct inspection. In conducting the antigen titrations and main tests I have used two units of hemolysin whereas Noguchi in his new test uses but one unit, unless hemolysis is incomplete when a second is added.

TABLE II

RESULTS OF TITRATION OF ANTIHUMAN HEMOLYSIN WITH VARIOUS HUMAN COMPLEMENT SERA\*

SERUM NO.	ANTI HUMAN HEMOLYSIN PAPER					
	2 mm.	4 mm.	6 mm.	8 mm.	10 mm.	25 mm.
25	S.H.**	M.H.	H	H	H	S.H.
36	S.H.	S.H.	M.H.	H	H	M.H.
44	S.H.	M.H.	H	H	H	H
46	S.H.	M.H.	H	H	H	H
58	S.H.	S.H.	H	H	H	S.H.
154	N.H.	S.H.	M.H.	H	H	M.H.

\*All sera from normal nonsyphilitic and Wassermann negative persons; used in constant dose of 0.1 c.c. within twenty-four hours after collection with 0.1 c.c. of 10 per cent suspension of human cells.

\*\*H = complete hemolysis; M.H. = marked hemolysis; S.H. = slight hemolysis; N.H. = no hemolysis.

Briefly stated Noguchi conducts his new test with 0.1 c.c. fresh human serum in each of two small test tubes to one of which is added 0.1 c.c. of 1:10 dilution of a suitable extract of acetone-insoluble lipoid antigen and sufficient salt solution to make the total volume 1.3 c.c. in each. After thirty minutes incubation on a water-bath at 37° C. the tubes are removed and to each are added 0.1 c.c. of a 10 per cent suspension of washed human cells and 0.1 c.c. of a dilution of the antihuman amboceptor representing one hemolytic unit. After reincubation for half an hour during which the tubes are shaken several times, the results are read. In case hemolysis is incomplete in the control tubes another unit of hemolysin is added and the tubes returned to the water-bath for half an hour.

Inactivated serum is used in dose of 0.2 c.c.; old serum not artificially inactivated in dose of 0.1 c.c.; in the case of cerebrospinal fluid 0.5 c.c. is employed. Human complement from a nonsyphilitic

person in dose of 0.1 c.c. is added and the test conducted after the usual manner. All tests are accompanied by controls with known positive and negative sera.

My work was conducted with fresh active sera as follows:

1. Only sera not over 24 hours old were employed; specimens of blood were usually collected during the afternoon and evening of the day before the tests were conducted and preserved in a refrigerator. On the following day the sera were secured and set up without delay in order to avoid deterioration of complement.

2. Into each of two small test tubes (10x1 cm.) was placed 0.1 c.c. of serum and into one of these (front tube) five antigenic units of an extract of acetone insoluble lipoids after preliminary anticomplementary and antigenic titrations as previously described. Normal salt solution was added to make the total volume 1 c.c. in each tube; the tubes were shaken and placed in a water-bath at 38° C. for thirty minutes, after which two units of amboceptor paper (the unit being determined as previously described) and 1 c.c. of 1 per cent suspension of human cells were added to all tubes, mixed and reincubated for half to an hour during which the tubes were gently shaken several times to interfere with the agglutination of the corpuscles.

3. At the end of half an hour if the antigen, hemolytic and serum controls were hemolyzed the results were read at once; if hemolysis was not complete in these or any of the serum controls of any particular test, the tubes were reincubated for another half hour. If at the end of this time the reading could not be made the test was discarded.

4. Known positive and negative controls were included and the front (antigen) tube containing the known negative serum served at the same time as the antigen control while the rear tube served as a hemolytic control in addition to a serum control on the negative serum.

5. In the majority of tests employing fresh active serum duplicate tests were made in the same manner employing 0.2 c.c. of each serum instead of 0.1 c.c., in an effort to sharpen the results.

I may also mention in this connection that I have used this technic with success as a complement-fixation test for gonorrhea; a polyvalent antigen was titrated in the same manner with known negative serum for anticomplementary unit and used in the main tests in an amount equal to one-third this unit.

Since the publication of Noguchi's paper I have also conducted a small number of tests (22) with cerebrospinal fluids employing the technic described by him.

The majority of specimens of serum were from persons in the Polyclinic Hospital and especially from the syphilis clinic of Doctor Jay F. Schamberg; for the purpose of special studies bearing upon the question of pseudo or falsely positive reactions with normal sera, specimens from numerous medical students and assistants were employed. Wassermann reactions employing three antigens, namely, an alcoholic extract of human heart reinforced with cholesterin, an alcoholic extract of syphilitic liver and an extract of acetone-insoluble lipoids, were conducted with all sera after heating at 56° C. for thirty minutes and used in dose of 0.2 c.c. with each antigen. In comparing the results of the Wassermann with the other tests, the Wassermann reaction was regarded positive if the reaction with cholesterinized extract was positive even though a serum reacted negatively with the alcoholic extract of syphilitic liver and extract of acetone-insoluble lipoids; this has an important bearing upon comparative results and I have learned from experience to place reliance upon results observed with properly prepared and titrated cholesterinized extracts.

#### RESULTS WITH THE NOGUCHI HOMOHEMOLYTIC COMPLEMENT REACTION

The results of 286 tests employing 0.1 c.c. active serum were as follows:

1. With 19 sera or about 7 per cent the Noguchi tests failed because of a lack of sufficient complement in the sera for the conduct of the tests.

2. Of the remaining 267 sera both the Noguchi and Wassermann reactions agreed insofar as the results were positive or negative with 246 sera or 92 per cent. Of these 267 sera, 243 were from hospital patients and the majority from the syphilis clinic; 8 were from persons suffering with scarlet fever and 16 were from medical students and assistants, whom we regarded normal and nonsyphilitic.

3. With 21 sera or 8 per cent the Noguchi tests were positive and the Wassermann reactions negative. This group requires further analysis by reason of the very important question regarding the possibility of pseudopositive or proteotropic reactions with active sera: 11 sera were from syphilitic persons undergoing active treatment

with arsphenamine and presumably the positive reactions with active serum may be interpreted as more delicate than the Wassermann reactions and regarded as specific; of the remaining 10 positive reactions, 8 occurred with the sera of hospital patients who were not regarded clinically or historically as syphilitic and 2 with the sera of medical students, who were presumably nonsyphilitic. Assuming that the 11 positive reactions with the sera of syphilitic persons under active treatment were all specific or true reactions, the Noguchi tests may be regarded as yielding about 96 per cent true reactions in this series and about 4 per cent presumably pseudopositive reactions. It is to be remembered that these tests were conducted according to the technic described, of which the prominent features were the use of purified extracts of acetone-insoluble lipoids titrated with human sera and the use of two units of hemolysin titrated with human complement. I believe that the percentage of pseudoreactions depends largely upon the question of antigen, inasmuch as crude extracts are apt to yield a higher percentage, and also upon the freshness and activity of the sera. *In this connection, it should be mentioned that six of the sera yielding pseudoreactions in the first tests, reacted negatively when repeated twice more with the same antigen and hemolysin and indicating that the differences were mainly due to the sera, as the technic was the same; I was unable to secure serum for repeat tests from the remaining four persons.*

4. All of the sera from scarlet fever patients reacted negatively in all tests.

5. With sera yielding weakly positive Wassermann reactions the Noguchi reactions were usually stronger.

6. With this series of tests, I did not encounter any sera yielding negative reactions with active sera and positive Wassermann reactions, and for this reason I regard the Noguchi test as particularly delicate serologic evidence of the absence of syphilis antibody in the body fluids.

As previously stated tests were also conducted with 0.2 c.c. active serum and employing the same dose of antigen and hemolysin, with the object of reducing the percentage of defective reactions due to insufficient complement in 0.1 c.c. serum and to sharpen hemolysis by increasing the activity of the hemolytic system; eighty-three sera were subjected to parallel tests employing 0.1 and 0.2 c.c. active serum and the regular Wassermann tests, with the following results:

1. All but three of the sera contained sufficient complement in 0.2 c.c. serum for the conduct of the test.

2. Of the 80 sera in which tests were made 70, or 88 per cent, yielded results agreeing with the Wassermann reactions so far as positive or negative were concerned.

3. With 7 sera, or about 9 per cent, the reactions with active serum were positive and the Wassermann reactions negative; none of these reactions occurred with the sera of persons regarded as non-syphilitic and, so far as can be determined, the results are true and indicative of greater delicacy. While it appears evident therefore that tests with 0.2 c.c. serum conducted with antigen and hemolysin adjusted to 0.1 c.c. serum, overcomes the tendency for pseudopositive reactions, I also observed 3 sera in this series from syphilitics under treatment, yielding negative reactions with 0.2 c.c. active serum, whereas with 0.1 c.c. serum and in the Wassermann tests the results were positive (with cholesterinized antigen alone in the Wassermann tests). Furthermore among the positive reactions observed with 0.1 and 0.2 c.c. of the same sera, the reactions with 0.2 c.c. serum were weaker in about 30 per cent. The larger dose of serum in this technic yielded therefore, no pseudopositive reactions so far as can be ascertained, but did yield a small percentage of falsely negative reactions and a large percentage of weaker positive reactions. At the present time I am continuing the work with the 0.2 c.c. dose of serum, but with the antigen and hemolysin adjusted to this amount instead of to 0.1 c.c. serum as, under these conditions, the results may prove more reliable.

#### RESULTS WITH INACTIVATED SERA AND CEREBROSPINAL FLUIDS

My results with inactivated sera and cerebrospinal fluids, employing normal human serum as complement, have not been nearly so satisfactory. The first experiments were conducted with 0.1 c.c. of 40 per cent dilution of human complement with 0.1 c.c. inactivated serum for diagnosis, but the percentage of indefinite reactions due to nonspecific inhibition of hemolysis in the main tests and controls was so large that subsequent experiments were conducted with undiluted human complement serum in various proportions as 0.1 c.c. and 0.2 c.c. complement with 0.1 and 0.2 c.c. inactivated serum; a combination of 0.1 c.c. complement serum with 0.1 c.c. heated serum for diagnosis appeared to yield best results inasmuch as 0.1 c.c. com-

plement serum with 0.2 c.c. heated serum yielded more nonspecific reactions and 0.2 c.c. complement with 0.2 c.c. heated serum no better results than the combination of 0.1 c.c. complement and 0.1 c.c. heated patient's serum.

The results of 88 tests conducted with the sera of 88 persons in dose of 0.1 c.c. heated serum with 0.1 c.c. normal human serum complement and otherwise with the same technic as used with active serum, were as follows:

1. With 21 sera, or about 24 per cent, the results could not be read owing to interference of hemolysis in the controls. None of these sera were anticomplementary in the Wassermann reactions and yielded correct positive and negative reactions.

2. Of the reactions with the remaining 67 sera, 52, or 85 per cent, agreed with the Wassermann reactions so far as the results were positive or negative; 10 sera, or about 14 per cent, yielded positive reactions with human complement and negative Wassermann reactions. Four of these sera were from nonsyphilitic medical students and the results were in all probability pseudoreactions; the remaining six sera were from syphilitics undergoing active treatment.

As previously stated 22 cerebrospinal fluids have been examined with Noguchi's technic, namely, in dose of 0.5 c.c. unheated fluid with 0.1 c.c. human complement serum, with these results:

1. With 9 fluids, or about 41 per cent, the results could not be read owing to nonspecific inhibition of hemolysis in the controls. All of these fluids yielded satisfactory positive and negative Wassermann reactions in dose of 0.8 c.c. unheated.

2. With the remaining 13 fluids, or about 60 per cent, the reactions agreed with the Wassermanns, although in several of these the controls showed slight interference with hemolysis. It must be stated in this connection that all of the fluids examined were from two to seven days old, but all were kept in a refrigerator and were perfectly clear.

My results therefore, with tests conducted with heated sera and unheated cerebrospinal fluids and human serum complement, were decidedly unsatisfactory and may have been due to a greater susceptibility of human complement to the anticomplementary activity of serum and cerebrospinal fluid, but I also believe that the results would have been better had I employed more powerful antihuman hemolysins inasmuch as similar tests with unheated sera and human



complement conducted at this time with antish sheep hemolysin and sheep cells (principle of the Health technic) yielded much more favorable results.

#### TECHNIC OF THE HECHT AND HECHT-GRADWOHL TESTS

As previously stated the Hecht technic<sup>5</sup> is based upon using the complement and antish sheep hemolysin of each patient's serum; therefore the test can be conducted if suitable antigen and sheep blood are available. As originally proposed and with later modifications, this test employs an alcoholic extract of guinea pig or human heart as antigen using 1 c.c. of 1:50, 1:100 and 1:200 dilutions with a constant dose of 0.1 c.c. fresh active serum. The fourth tube of each series serves as a serum control. After a primary incubation of half to one hour, 1 c.c. of a 2 per cent suspension of sheep cells is added to all tubes followed by reincubation for one to two hours. No directions are given for determining the proper dose of antigen and the dose of corpuscles is purely arbitrary and based upon the observation that the majority of fresh human sera in dose of 0.1 c.c. contain sufficient hemolysin and complement to hemolyze this number of cells. In the event this does not prove true with an individual serum, the test is worthless.

In my experience this test has proved of little value because the dose of cells is too large for a large percentage of sera and the crude antigens yield too many falsely positive or pseudoreactions. But the first error has been corrected by Gradwohl's modification<sup>6</sup> which measures the hemolytic activity of each serum and grades the dose of cells accordingly, and the second error is corrected with the use of purified antigens of acetone-insoluble lipoids titrated for anticomplementary and antigenic activity with active normal and syphilitic sera respectively. With these changes, I found the Hecht-Gradwohl test very satisfactory and the test of choice for employing human complement<sup>9</sup>. Since the publication of my paper, I have performed parallel Hecht-Gradwohl and Wassermann tests with 190 sera, using the following technic for the former test:

1. Only perfectly fresh sera were employed; specimens sent in the mails from a distance or over forty-eight hours old were frequently unsatisfactory.

2. Only purified extracts of acetone-insoluble lipoids titrated with human sera as previously described<sup>9</sup>, were employed as antigen.

3. Seven small sterile test tubes ( $10 \times 1$  cm.) are arranged for each serum and into each is placed 0.1 c.c. of fresh unheated serum. To the first five tubes are added respectively 0.1, 0.2, 0.3, 0.4 and 0.5 c.c. of a 5 per cent suspension of sheep cells; to the sixth tube is added five antigenic units of extract and the seventh tube serves as the serum control. Sufficient normal salt solution is added to each tube to bring the total volume to 1.0 c.c.

4. All tubes are gently mixed and placed in a water-bath at  $38^{\circ}$  C. for half an hour when the hemolytic index (largest amount of corpuscles just completely hemolyzed) of each serum is read and one-half the indicated dose of cells added to the sixth and seventh tube of each series. The tubes are gently mixed and *reincubated for about half an hour according to the hemolysis of the controls. Hemolysis in antigen, serum and negative controls is usually quite prompt and active, and the results are read as soon as these controls show complete hemolysis.*

5. Tests with a known normal and if possible, with a known syphilitic serum are included; the sixth and seventh tubes with the normal serum serve not only as a negative serum control but as antigen and hemolytic controls respectively. During the past year, I have also used this technic with success as a complement-fixation test for gonococcus infection; the antigen is titrated with normal serum alone and used in the main tests in dose corresponding to one-third the anticomplementary unit.

#### RESULTS WITH THE HECHT-GRADWOHL REACTION

With this technic I have found that at least 92 per cent of sera are satisfactory for the test and only a few sera contain sufficient complement and amboceptor to hemolyze more than 0.5 c.c. of a 5 per cent suspension of cells so that larger doses are not required in determining the hemolytic indices of the sera in the routine tests.

The results of Hecht-Gradwohl and Wassermann tests with 190 sera, are as follows:

1. With 15 sera or 7 per cent the hemolytic activity was too weak for the conduct of the Hecht-Gradwohl test.

2. With the remaining 175 sera the results agreed with the Wassermann reaction so far as positive or negative were concerned with 150 sera, or about 85 per cent.

3. With 22 sera or 12 per cent the Hecht-Gradwohl tests were

positive and the Wassermann reactions negative with all antigens. In every instance the history, clinical diagnosis, or both, justified a diagnosis of syphilis and indicated the superior delicacy of the Hecht-Gradwohl test; the majority of sera were from syphilitic persons under active treatment.

4. With 3 sera or from 1 to 2 per cent of the total the Hecht-Gradwohl tests were negative and the Wassermanns positive; with the sera of two of these patients the tests were repeated about one week later with positive results in both. I can not explain the occurrence of these negative Hecht-Gradwohl reactions; all sera were from syphilitics under active treatment but their occurrence shows their possibility in the conduct of the test under routine conditions.

These results are quite similar to those previously reported in which the Hecht-Gradwohl and Wassermann reactions yielded similar results with 82 per cent of 360 sera. In the former series I found 6 sera, or about 2 per cent, yielding positive Wassermann and negative Hecht-Gradwohl reactions and in the present series a similar result was observed. While in the former series 2 sera yielded pseudopositive or proteotropic reactions, none occurred in the present series, a result which I ascribe to the use of acceptable extracts of acetone-insoluble lipoids as antigen after titration with human instead of guinea pig complement.

I have attempted to simplify the Hecht test by using a constant dose of 0.1 c.c. of a 5 per cent suspension of sheep cells routinely with each serum instead of one-half the hemolytic index of cells as in the Hecht-Gradwohl technic. The result of these tests have shown that with many sera this dose of cells is too small and falsely negative reactions occur with syphilitic sera due to the presence of sufficient unbound complement and hemolysin to effect complete hemolysis. Wassermann and Hecht tests with this technic conducted with 180 sera yielded the following results:

1. Both tests agreed with 140 sera, or in 78 per cent.
2. With 26 sera, or about 14 per cent, the Hecht tests were negative and the Wassermann weakly positive; all of these sera were from syphilitics under treatment and the negative Hecht reactions are probably to be ascribed to a too small dose of corpuscles.
3. With 14 sera, or about 8 per cent, the Hecht tests were positive and the Wassermann tests negative; all sera were from syphilitics under active treatment and probably occurred with sera which

happened not to be actively hemolytic and indicating the superior delicacy of tests conducted with active serum, provided the dose of cells is correct.

SUMMARY AND CONCLUSIONS REGARDING THE PRACTICAL VALUE OF THESE  
TESTS UNDER WAR CONDITIONS

The particular value of the new Noguchi and Hecht-Gradwohl tests under war conditions is dependent largely upon their simplicity and the utilization of human complement; the former requires human corpuscles and antihuman hemolysin while the latter may be conducted if sheep corpuscles are available. Since the importance of reliable complement-fixation tests for syphilis and to a lesser extent for gonococcus infections, in diagnosis and as controls on treatment and indices of cure is definite and emphatic, the main question at issue regards the delicacy and reliability of these tests as substitutes for the Wassermann reaction. The comparative results are expressed in the body of this communication by figures and percentages; here general conclusions alone may be briefly given.

In the first place both tests conducted with active serum are very delicate and serve to detect syphilis antibody under conditions in which the Wassermann reaction may be negative even with cholesterin-reinforced antigens. For this reason I regard a *negative* Noguchi and Hecht-Gradwohl reaction better evidence of the absence or cure of syphilis than a negative Wassermann.

Of greater importance is the question of pseudo or falsely positive reactions which may result when active serum is employed and particularly under the conditions of these tests in which each patient's own serum is used as complement. In my experience the Hecht-Gradwohl test when conducted with an acceptable antigen of acetone insoluble lipoids titrated with active human serum, is particularly reliable in this respect, although I still check up the positive reactions with a Wassermann and use the test upon request as a control over the Wassermann. With the new Noguchi test employing 0.1 c.c. of active serum, I found from 1 to 4 per cent pseudo-reactions which are ascribed more to slight deterioration of complement or weak hemolysin than to proteotropic reactions due to defective antigen, inasmuch as a repetition of such tests with fresh sera are apt to yield negative reactions. Noguchi homohemolytic tests conducted with 0.2 c.c. serum yielded no falsely positive reactions but

gave too many falsely negative results owing to the excess of complement present under the conditions described in this paper.

My results with Noguchi's new test employing inactivated sera and cerebrospinal fluids with human complement, were decidedly unsatisfactory by reason of the occurrence of a high percentage of anticomplementary or indefinite reactions. In my experience the test is better conducted with active serum and cerebrospinal fluids should likewise be fresh and well preserved.

The necessity of using perfectly fresh sera in both the Noguchi and Hecht-Gradwohl tests for the best results, constitutes an objection of more or less weight depending upon circumstances, inasmuch as specimens must be collected on certain days or the tests conducted almost daily.

In the Noguchi as in the Hecht-Gradwohl test, antigen of acetone insoluble lipoids is most reliable and particularly from the standpoint of pseudo or falsely positive reactions; in my opinion the antigen for both tests should be titrated at frequent intervals with human serum instead of with guinea-pig complement. In the Noguchi test it is very important to use as powerful antihuman hemolysin as possible in order to avoid the disturbing factor of hemagglutination and the difficulty of preparing sufficiently active hemolysin may constitute a drawback to the test. For this reason, I prefer the Hecht-Gradwohl test and believe it to be the technic of choice when employing human complement, if sheep cells are available.

The technic of the Noguchi homohemolytic and Hecht-Gradwohl tests has been successfully applied in the diagnosis of gonococcus infection in a small series of cases.

The final acceptance of either of these tests as substitutes for the Wassermann reaction will depend largely upon the experience of individual serologists; to those experienced in the conduct of the Wassermann reaction they are likely to be accepted more as controls than as routine tests. At the present time I believe that either may be used routinely provided proper antigen is available and sufficiently active hemolysin for the Noguchi tests, but that positive reactions should be repeated and then checked up with a Wassermann and that the latter should be available for testing the 8 per cent of sera which contain too little complement or hemolysin or both for the conduct of either test using the patient's own serum for complement.

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# AN ENDEAVOR TO INCREASE THE POTENCY OF LOW TITER ANTISHEEP AMBOCEPTOR BY MEANS OF CHEMICAL FRACTIONATION

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MANY methods have been proposed for the production of anti-sheep amboceptor in rabbits, different workers putting forth this or that procedure as giving remarkable titers in a short time. We have found, however, in our routine immunization of large numbers of animals, that apparently the individual susceptibility of the animal plays an important part in obtaining satisfactory results.

A high titer serum is desirable for a number of reasons, not the least of which is its greater economy for use in a large number of tests. Unfortunately many rabbits will not easily give a titer of more than 1:500, while for the routine Wassermann test we require a titer of at least 1:1500; that is to say, a serum 0.05 c.c. of which in a 1:1500 dilution will produce complete hemolysis of 0.1 c.c. of 5 per cent suspension of washed sheep cells in the presence of .1 c.c. of 10 per cent complement at the end of one hour in a water-bath at 37° C.

In our work we had accumulated a number of amboceptors with titers of from 1:300 to 1:500 and it occurred to one of us (Gilbert) that if by some means the fraction containing the immune body could be separated from the inert portion of the serum, it might be possible to increase the potency of such sera so that they could be used after fractionation.

In this connection the work of Müller<sup>1</sup> and Pick<sup>2</sup> to whose work Müller refers, gave suggestions which we applied to a preliminary study of the results of fractionation of antisheep amboceptor. Müller and Pick found that the euglobulin and pseudoglobulin fractions of immune blood sera contained all of the following antibodies: cholera lysin, typhoid agglutinin, cholera agglutinin, streptococcus agglutinin, and lacto-precipitin. Müller gives the following table which shows the plasma fractions of the different animals studied, containing these antibodies:

TABLE OF RESULTS OF MÜLLER'S WORK

Immune body	Fibrin globulin	Euglobulin	Pseudo-globulin	Albumin
Diphtheria antitoxin	0	Goat	Horse	0
Tetanus antitoxin	0	Goat	Horse	0
Cholera lysin	0	Goat	0	0
Typhoid agglutinin	0	Goat		
		Rabbit	Horse	0
		G. pig		
Cholera agglutinin	0	Goat		
		Horse	0	0
Streptococcus agglutinin	0	Horse	0	0
Lacto-precipitin	0	Rabbit	0	0

After we had completed our tests Kosakai<sup>3</sup> published a method of isolation, purification, and concentration of antisheep amboceptor. His procedure is as follows: To a 1:100 dilution of inactivated antisheep amboceptor in physiologic salt solution, add enough washed sheep's red blood cells to absorb the amboceptor. Centrifugalize and discard the supernatant fluid. Suspend the amboceptor red blood cell combination in 10 per cent saccharose solution and shake to separate the amboceptor from the red blood cells. (About 5% of the amboceptor can be removed.) Centrifugalize to remove the cells. Shake with ether to remove traces of hemoglobin. Dialyze the saccharose amboceptor mixture to remove the sugar. Finally, concentrate the purified amboceptor in an exsiccator. It would be very difficult to prepare large amounts of amboceptor by this procedure. Kosakai devised the method for the production of small amounts of really pure amboceptor, and did not plan to use it for a routine method to prepare a sufficient quantity for Wassermann tests.

Taking the work of Müller and Pick as a basis for our experiments we selected a number of different sera of titers ranging from 1:300 to 1:500. We pooled these sera and titrated the mixture. We obtained complete hemolysis with 0.08 c.c. of the 1:300 dilution. The globulin fraction was then separated by means of precipitation with ammonium sulphate. This fraction gave, when titrated, complete hemolysis through 0.05 c.c. of a 1:500 dilution. The albumin fraction gave no hemolysis even with 0.1 c.c. of the undiluted material; 1:300 and 1:500 dilutions of this fraction were also tested with the same result.

Further separation of the globulin fraction into pseudoglobulin and euglobulin gave, upon titration, complete hemolysis with 0.08 c.c. of a 1:500 dilution of the pseudoglobulin and complete hemolysis with from 0.02 c.c. to 0.01 c.c. of the undiluted euglobulin, thus showing



that, although most of the immune body is apparently contained in the pseudoglobulin fraction, enough is contained in the euglobulin fraction to make a union of the two desirable and therefore to render it unnecessary to separate the two globulin fractions.

If the globulin has become too dilute while dialyzing, the excess of water may be easily removed by the Kober<sup>4</sup> method of pervaporation. The dialyzing bag may be hung in front of an electric fan until the globulin is sufficiently concentrated.

From these results it seems possible to increase the potency of low titer antisheep amboceptor by removing the inert albumin fraction.

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## ON THE DEBATABLE PHASES OF THE WASSERMANN TECHNIC

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SINCE the application of the complement-fixation phenomenon of Bordet by Wassermann and his associates in 1906 in the diagnosis of syphilis, the addition of certain refinements to the test have advanced considerably the diagnostically specific status of the reaction. Of these, the demonstration by Landsteiner and his coworkers that alcoholic extracts of guinea pig hearts were more antigenic and less anticomplementary than aqueous extracts of luetic livers, the fortification of alcoholic extracts with cholesterol suggested by Sachs, the introduction of the titration of complement instead of amboceptor by Boas, the demonstration of the greater fixability of complement in low than in high temperature by Jacobsthal, and the discovery of the dual character of complement relative to fixability and hemolysis, and the quantitative determination method of complement fixation by Browning and McKenzie have brought about a delicacy in reaction far removed from the original conception of Wassermann.

Nor am I unmindful of the apparently minor technicalities introduced into the reaction by Citron, Boas, Noguchi, Thomson, Ottenberg and others. It is above all else that fastidiousness and unrelaxing zeal in regard to detail that makes or unmakes the dependability of the work of the individual serologist.

No more gratifying and assuring evidence of the evolution of the reaction and its stabilization is shown in the dependable statistics gathered in the various technical periods of the reaction and its influence upon the conception of syphilology in general. Unfortunately, the lack of coordination and technical detail in published statistics renders these in most instances unfit for comparison. Especially is this true during the earlier years of the reaction and it is regretted that many of these first reports stand today as indices of the diagnostic application of the test.

## REPRESENTATIVE STATISTICS AND STANDARDS OF THE WASSERMANN REACTION AT VARIOUS PERIODS

	1909	1912	1914	1918
	PASTEUR INSTIT. (ORIG. METHOD. ALC. EX. ANTGN.)	COMPILED BY NOGUCHI (ORIG. METHOD. ALC. EX. ANTGN.)	BOAS (TITRATION OF COMP.)	LARKIN, LEVY AND FORDICE (TIT. OF COMP. CHOLEST. ANTGN. WARM. PLAIN COLD.)
Primary	-	69%	73%	(on age of lesion 95-100%
Secondary	92%	89.4%	{ Untreated 100% Treated 94% (relapse)	100%
Tertiary	63%	(manifest) 78.1%	(untreated) 97%	{ Late skin &m.m. 94% Visceral (pl. ant. warm) 94%
Latent	-	{ Early 51% Late 47%	Treated 39% Treated 47%	
Paresis	70%	88.1%	100%	99%
Tabes	60%	62.6%	{ Untreated 100% Treated 45%	50%

There has also developed, with the control of the too great flexibility of the original test, an increasing value of its negative deductions. The absence of complement fixation with a cholesterinized antigen speaks strongly for the exclusion of syphilis.

On the other hand, with the increasing accuracy of the test in bringing to light every phase of syphilitic possibility, the question of overstepping the limits of such probability must not be overlooked. It is of course easy to place the onus of interpretation upon the clinician with suggestive positive reactions but I have often found this course as misleading and vitiating the importance of the test in general rather than being diagnostically helpful. My own inclination is to embrace any suggestion or modification that might enhance the reaction's delicacy, but I am equally conservative in rejecting any change that tends to indict the nonsyphilitic.

Many modifications or substitutes for the Wassermann reaction have been suggested. Too often have individually conceived methods, at times in contravention to fundamental principle, been masqueraded as the Wassermann technic. Usually these have been done with the idea of saving time and introducing short cuts in technic. Had the original reaction received such attention in detail elucidations as has

been spent in originating and exploiting rather radical digressions there would not have arisen that skepticism indulged in by a considerable number of medical men.

#### CONCERNING COMPLEMENT

In the use of guinea pig serum for its complement content it can be categorically stated that the serum should be collected from healthy grown pigs; that the serum be allowed to spontaneously separate from the clot without manipulation or centrifugalization lest by mechanical injury to the cells a lipoidal substance be freed which in the presence of other lipoids (antigen) exercises in itself a binding power on complement; that drawn serum, when kept at low temperature usually ascends in dynamic character for several hours, maintains this curve for from 12 to 24 hours and weakens more or less rapidly according to the conditions under which it is kept; even when frozen it loses in power, and, as is the character of all serums, there develop substances inimical to its own action; that the preservation of pig serum with sodium chloride does not maintain its full complemental power nor does it prevent the development of substances in themselves anticomplementary; that its complement strength is highest in concentration and is vitiated or even dissipated by certain degrees of dilution, therefore fluid constants must be maintained in all determination involving the action of this body.

*The fixed dose of complement (0.1 c.c.) entering into the original Wassermann system allows a fairly constant relationship between the hemolytic factors concerned.*

This method of hemolytic system titration is still in vogue, probably on account of the time factor and the premise of quantitative relationship of complement and amboceptor in the induction of hemolysis. It will be shown, however, that this conception disregards certain other important phases of complement deviation.

In a series of 1405 hemolytic systems titrated by this method, amboceptor against 0.1 c.c. complement, with pooled and individual pig serums, original amboceptor unit being 0.00015 c.c., I found the unit to be

0.00005	42 times
0.0001	223 times
0.00015	615 times
0.0002	335 times

0.00025	118 times
0.0003	22 times
0.0004	11 times
Uncomplementary	39 times

*One tenth c.c. of guinea pig serum represents two or more units of complement.*

Boas<sup>1</sup> finds the complement unit of fresh pig serum to be between 0.04 and 0.07 c.c. Stillians<sup>2</sup> in 10 titrations with 4 per cent corpuscle suspension finds it to be 0.015 to 0.025 c.c. Ottenberg<sup>3</sup> finds the serum more frequently overactive than underactive and concludes that in 0.1 c.c. serum there are frequently 3 or more complement units. Van Saun<sup>4</sup> finds the reverse to be the case and seldom finds a mixture of pig serum that titrates higher than a 1 in 10 dilution and usually about 1 to 8.

In a series of titrations—complement against two units of amboceptor—it was noted by me that the usual complement titer was 0.04 c.c., rarely above 0.08 c.c. The average complement titers of 100 consecutive pigs was 0.047 c.c. Not included in this series are the serums of two pigs which failed to hemolyze in doses of 0.1 c.c. In pooling pig serums I first determined the approximate individual titer, discarding low serums. The titer of the pool equals the average of the individual titers.

From this it is obvious that in the majority of instances the Wassermann dose of complement (0.1 c.c.) contains  $2\frac{1}{2}$  units. On the other hand, workers with the Wassermann method of titration not infrequently have a reserve of complement so scant as to allow little margin for anticomplementary factors.

Fortunately, as will be considered later, the anticomplementary action of antigen and human serum, with proper adjustment and handling, is almost entirely negligible. The real liability of error in this method is considerable when weak binding serums are tested with pig serums of several complement units leaving one or a large fraction of one free unit for ultimate cooperation with amboceptor.

Since Browning and McKenzie<sup>5</sup> demonstrated the duality of complement in that its hemolytic strength was not an index to its flexibility with syphilitic "antibody" and antigen, serologists have generally failed to heed this highly important warning. Ottenberg has found a considerable degree of variation in the fixability of different pig serums. With dilutions of an identical luetic serum various com-

plements showed from one to four times the amount of fixation. The suggested means for overcoming this by the use of pooled pig serums does not appear adequate in that the selection might include a larger portion of complement of low fixability. The determination of the fixability of individual serums by titrations with pooled positive serums appears to me more logical.

Stillians maintains that complement loses in fixability before it does in hemolytic strength. With complement preserved with salt and refrigeration (5 to 10 e.c.) he found fixability considerably reduced in eight of twenty-six serums. Some of these serums were relatively fresh while others were kept for various short periods to twelve days. Some complement kept fourteen days still held its fixability. In determining this point with unsalted serums kept at the usual ice box temperature I have found the titer of hemolytic complement diminish in greater degree than does its fixability. As an example in point, the complement titer of a given serum was .04 in 18 hours, .06 in 48 hours, and .08 in 96 hours. Two units of the 18-hour titer were completely fixed by .03 e.c. in 20 hours, by .03 e.c. in 48 hours, and by .05 in 96 hours, of a given positive serum. Unless pig serum be preserved I do not feel that a possible lowering in fixability need concern us.

#### FACTORS GOVERNING THE ESTABLISHMENT OF THE HEMOLYTIC SYSTEM

*The establishment of the hemolytic system for fixation tests is in reality the determination of the titer of complement with two units of a high titer amboceptor serum plus that amount absorbed by the various factors entering into the test.*

I have noted of late that many workers use an amboceptor of relatively low titer with apparent impunity. I have always feared the introduction of many large serum factors in the test and have empirically accepted 0.002 e.c. of immune rabbit serum as the lowest permissible hemolytic unit. All serums develop anticomplementary bodies with age. Especially as amboceptor serum is kept for months or years, this factor may become considerable. By holding the amboceptor serum to very minute doses the developed anticomplement is not appreciated.

In previously considering the titer of complement it was by the immediate assembly of the three factors concerned in the hemolytic reaction, diluted to 5 e.c. When, however, other factors are introduced, to determine the noninterference, reduction or nullification of this

phenomenon by one of these factors, namely, its binding effect on complement, certain other factors are also introduced in a measure interfering with the proper determination of either or both of these reactions.

In the test proper the titer of complement is influenced by the conditions under which fixation is determined and is variably influenced by the antigen used and human serum.

*When the fixation test is performed entirely in the warm, (air thermostat on water-bath 37.5° C.) the conditions under which complement is titrated must absolutely simulate the conditions under which the final test is performed.*

Liefmann and Cohn have called attention to the rapid deterioration of complement at 37° to 40° C. especially when in dilution, and Browning and McKenzie have emphasized the need of performing the pre-test titrations under conditions similar to that of the test itself.

I have found the titer of complement as determined by the immediate incorporation of all the test factors to be as a rule considerably higher than when complement remains in solution alone at 37.5° C. for the fixing period of the test proper before the addition of amboceptor and cells.

Parallel titrations of complement of a representative serum by the immediate and interrupted methods will appear in the following ratio:

FULL TEST—AMBOCEPTOR 2 UNITS—1 HR. AIR THERMOSTAT

Complement	.08	.07	.06	.05	.04	.03	.02
Immediate titration	+	+	+	+	±	±	±
Interrupted “	+	+	±	±	±	±	—

( + complete hemolysis)

It is generally considered that antigen exercises some anticomplementary action even in contradiction to the rule that antigen is not anticomplementary. The reason for this attitude of serologists is that a discrepancy occurs in the unit of frank hemolytic system titration and titration in the presence of antigen, by interruption. Baos finds that a complement giving a titer of 0.05 without antigen gives a titer of 0.08 with antigen. McIntosh<sup>6</sup> found the serum of 3 pigs out of 24 as being hypersensitive to antigen and became completely deviated by it. He considers such serums as unsuited and rejects them. I have never observed such an affinity and would be inclined to place the blame on antigen rather than complement, provided however, that the serum was complementary in the ordinary system.

Contrary to the accepted idea, I find antigen of plain alcoholic extract as never being anticomplementary when reagents are immediately assembled, and even the reverse. The subhemolyzed tube by the plain system is often completely hemolyzed in this tube with antigen. Nor do I find the cholesterinized extract to be anticomplementary although the subhemolyzed tube of the plain system is never affected.

Another titration of the above complement, parallel immediate and interrupted titrations with antigen, that is the immediate collection of all reagents and the exposure of dilute complement to the test dose of antigen for one hour in thermostat before addition of amboceptor and cells, appears to give practically the same results.

WITH PLAIN ALCOHOLIC EXTRACT ANTIGEN

Complement	.08	.07	.06	.05	.04	.03	.02
Immediate titration	+	+	+	+	+	≠	≠
Interrupted "	+	+	≠	≠	≠	—	—

WITH CHOLESTERINIZED ALCOHOLIC EXTRACT ANTIGEN

Complement	.08	.07	.06	.05	.04	.03	.02
Immediate titration	+	+	+	+	≠	≠	—
Interrupted "	+	+	≠	≠	≠	—	—

( + complete hemolysis)

Human serum is one of the most uncertain factors entering into the test and is influenced by its lipid content, the method by which the serum is recovered, its age and sterility, and the degree and recentness of its inactivation. Fresh, recently inactivated serum has generally no anticomplementary action. Pooled negative serums are generally not less than 24 or 48 hours old and have acquired more or less anticomplement.

Titration of the above complement in the presence of pooled negative serum (free from native hemolysins) and without antigen shows the following variation:

WITH POOLED NEGATIVE SERUM (0.2 C.C.)

Complement	.08	.07	.06	.05	.04	.03	.02
Immediate titration	+	+	+	≠	≠	≠	—
Interrupted "	+	+	≠	≠	≠	—	—

( + complete hemolysis)

Titration of complement in the presence of pooled negative serum and alcoholic extract antigen and cholesterin-fortified antigen gave the indential result as the titration with negative serum above in



both instances. Ottenberg finds the influence of antigen and pooled negative serum to be but slight—only 0.005 c.c. being necessary over the plain titer. Thomas and Ivy<sup>7</sup> find the titer of complement with antigen and 0.1 c.c. pooled negative serum about 0.05 c.c. and the plain titer about 0.04 c.c.

## UNIT OF COMPLEMENT DETERMINED

	IMMEDIATE (All factors assembled)	INTERRUPTED (Factors of fixation phase 1 hour at 37.5° before addition of cells and ambo.)
Simple hemolytic system	.05	.07
With plain alc. ex. antigen	.04	.07
With cholest. " "	.05	.07
With pooled neg. serum (0.2)	.06	.07
With neg. serum & plain antigen	.06	.07
" " " cholest. antigen	.06	.07

## SUMMARY OF COMPLEMENT TITRATIONS

Similar titrations to the foregoing have been performed by me repeatedly and have usually demonstrated the marked reduction in the hemolytic action of complement when exposed in dilution (1:10) to 37.5° C. for the hour period of fixation before amboceptor and cells are added. Antigen (plain extract) seems to enhance the action of complement when immediately assembled with it rather than decrease it. With individual fresh human serums I have rarely noted anti-complementary action. Old serums or pooled serums are always more or less anticomplementary. In fact in the thermostat method of fixation it is this thermal effect upon complement that brings about the reduction of the titer rather than absorptive action of fresh human serum.

The test unit of complement determined in this manner is often twice the actual Bordet unit. Workers who assume that they are using two units of complement, when complement is titrated immediately, even in the presence of antigen and negative serum, in their test proper are often using but one full complement unit. Should two such units be put in the final test an obviously unbalanced system would be brought about.

*When the fixation period of the test is performed in the cold (8° to 10° C. for 4 hours) the conditions under which complement is*

*titrated needs simulate the conditions under which the final test is performed only in the immediate addition of antigen and human serum.*

Titration of complement in the immediate presence of alcoholic extract antigen, fresh negative serum, amboceptor and cells, is equivalent to titration by interruption. Check titrations have failed to indicate any greater absorption of complement when the first phase factors are exposed to each other for the first hour period in the ice chest before the addition of amboceptor and cells, than when assembled from their various containers.

The titer of complement so determined will be found to vary but slightly from the titer of the immediate simple hemolytic system and about half the dose as determined by warm fixation.

*Inasmuch as the minimal amount of complement necessary for bringing about a complete end reaction is demanded for the test, this titer must be determined at its apex of capacity.*

Most workers fix an arbitrary time for titration readings. Some read and accept the 15 units titer while others do not declare the units until after a 2 hour lapse.\* With daily observations of the titration of hemolytic systems it must be noted that various systems, under identical conditions, do not react with the same velocity nor do they reach height of hemolytic activity at the same time. A certain system may show an early rapidity in action and slow up in 30 minutes, there being but slight advance at the hour period, while another system may show but slight progress at the 30 minute period and pick up a considerable energy in the last half hour. It must, however, be emphasized that dissociation factors must set a time limit to the reaction. I am inclined to think that I get more even results with the air thermostat in one hour than I do in the water-bath for half that period.

What applies to the hemolytic system proper applies also to the warm exposure of the final phase of the fixation test. The same thermal conditions must be maintained with both systems. A mere time for time stay in the warm does not suffice. Either the racks, tubes and contents must be the same temperature on being placed in thermostat or water-bath or if considerably colder for the last incubation the temperature of the environment must be raised to

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\*It is of course understood that in this discussion we are confining ourselves to the separate additions of amboceptor and cells, and proper deductions must be made when sensitized cells are used.

bring about a rapid warming of the fluids. Smith and MacNeal<sup>8</sup> in the last phase of the reaction after ice box fixation adjust the water-bath temperature at 45° C. This falls to 37° C. at the end of fifteen minutes, readings being made in thirty minutes.

#### CONCERNING ANTIGENS

In the maze of Wassermann controversy no one factor has been buffeted as has antigen. In efforts at standardizing the reaction the antigen arises as the real bone of contention and no two workers appear to meet on common ground. Its character, its method and degree of dilution and its titer and quantity entering into the test seem to appeal variously to different workers. The recent trend, however, is encouraging in that it is generally conceded that antigens of different character have a various adaptability.

Of the three types of antigen in present use, namely, the organ alcoholic extracts (usually heart), the cholesterin fortified alcoholic extracts and the acetone-insoluble lipid, the plain alcoholic and cholesterinized appear to be the antigens of choice. Since the introduction of the ice chest method of fixation the plain extracts have surpassed the acetone-insoluble lipoids in antigenic delicacy and have maintained their less anticomplementary character. As a result the Noguchi antigen is no longer in vogue except as a conjunction antigen and is preferred by some as the extract for cholesterin fortification. *Antigen, of whatever character, must meet specific qualifications before it can be used as a test reagent.*

Antigen, viewed in the light of a colloid, appears to possess a greater fixing power when its molecules are in a certain degree of dispersion. When the molecule aggregates are too large, it is likewise anticomplementary. An optimum degree of emulsion, however, exists wherein its opacity continues in increasing dilution. By the slow addition of saline solution to the alcoholic extract this opacity can be sustained until a dilution of from 1:10 to 1:15 is reached. Each extract seems to possess an individual opacity index and I consider it advisable to dilute various extracts accordingly. The fixed 1:10 or 1:20 dilution of extract is the common practice. Detweiler<sup>9</sup> instead of using fractions of a given dilution uses in his titrations a series of antigen dilutions. ✓

The basic requirement of antigen is that it be strongly antigenic in small doses but not in the least anticomplementary in large doses.

The original Wassermann dictum is that one half of the largest dose that in itself is not anticomplementary should completely deviate 0.1 c.c. of complement with 0.1 c.c. of positive serum. Ottenberg points out that this amount prescribed by Wassermann will, with a good antigen, contain from five to ten antigen units or be five to ten times as large as the dose necessary to give completely such fixation.

Most workers arbitrarily use a friction, from  $\frac{1}{4}$  to  $\frac{1}{2}$ , of the beginning anticomplementary or largest non-anticomplementary dose, provided it meets antigenic requirements. With cholesterinized antigen a smaller fraction is used or a looser hemolytic system is allowed for the excess of anticomplementary action, although Sachs uses  $\frac{1}{2}$  the largest non-anticomplementary dose.

Ottenberg thinks that the arbitrary dose of antigen is not necessarily the optimum one. He found that a given antigen, with complement adjusted to it, did not give the degree of fixation in large doses as it did in smaller amounts. He explains this by assuming that after a certain dose its anticomplementary effect increases in greater ratio than does its antigenic effect. He has therefore reduced the amount of antigen used by him in his tests—about one-half that used by Thomas and Ivy—with actually better results. Smith and MacNeal (using  $\frac{1}{5}$  test with fixed complement) find the smallest antigenic dose to vary according to the character of antigen and the method of fixation. A plain extract antigen fixed complement with strongly positive serum in dose of 0.05 c.c. of a 10 per cent emulsion by warm fixation while the same fixation occurred in the cold with 0.2 c.c. of a 1 per cent emulsion—being two and one-half times stronger. Likewise was the cholesterinized antigen stronger by cold fixation in ratio of 2 to 1, the minimal doses being respectively 0.1 and 0.2 of a 1 per cent emulsion. They use 0.1 c.c. of emulsion of all antigens in their tests although they do not state what the emulsion percentages are. Detweiler (using  $\frac{1}{2}$  test 3 units complement—1 c.c. pooled positive serum—warm fixation) titrates antigen for binding power in a series of dilutions from 1:30 to 1:40 and low dilutions for anticomplement, 0.5 c.c. being in each tube. He rules that antigen must not be anticomplementary with 0.5 c.c. of a 1:8 dilution and must give complete fixation with this amount of a 1:80 dilution. For the test he chooses a dose usually midway between the lowest binding and lowest anticomplementary dilution.

My first concern with a new antigen is a rough determination of its antigenic power, as all extracts are not of equal potency and I have discarded a half dozen consecutively prepared extracts because the titer did not compare favorably with the titer of the antigen in use. When favorable, its minimum titer is determined by daily titrations with positive serums (0.1 c.c.) for a week's time. This allows an appraisal of its fixing power with about 20 positive serums of different "antibody" content. This unit, with an acceptable antigen, varies between 0.05 and 0.1 c.c. I arbitrarily use two such units in the tests, warm or cold fixation, provided that it is not anticomplementary in 4 such units. It is rarely anticomplementary in 8 such units. Detweiler (figures transcribed) finds 0.4 c.c. of 10 per cent emulsion the usual beginning anticomplementary amount. MacNeal (using  $\frac{1}{5}$  system) finds a plain alcoholic antigen not in itself binding in dose of 0.4 c.c. of 10 per cent emulsion but that when fortified with cholesterin this amount becomes anticomplementary. Also, that cholesterinized extract increases in anticomplementary action with age, especially in ice box fixations. McIntosh considers that the anticomplementary element in antigen is the alcohol and that in dilution of 1:15 it has practically no inhibiting power at all. I have confirmed this, and have found only a slight increase in anticomplement with cholesterin alcohol at this dilution. Fortunately, the lower fixing titer of cholesterin antigen obviates this increased anticomplement factor.

*Plain and cholesterinated antigens are variously adapted in diagnosis and the use of one to the exclusion of the other denies the test its fullest value.*

Most serologists are unfortunate in not having a knowledge of the clinical possibilities of the cases referred to them for complement fixation study. To many clinicians a Wassermann is a Wassermann and the finer test differences are to them unknown. Yet the diplomatic serologist can often subtly create a clinical attitude without appearing to be overintrusive. A serum reported as positive with one antigen and negative with another, unless such report is accompanied by general explanations, often leads to dire confusion. I have found it helpful, when without the clinician's confidence, to insert with reports a brief discussion of the test values of the various antigens and methods used.

That cholesterin-fortified antigen is more delicate than the plain

extract is universally accepted. Ottenberg<sup>10</sup> finds a difference of 15 per cent between the two. It has also been shown that it gives a higher percentage of true and false fixations at low than at high temperature. Smith and MacNeal in a series of untreated clinically positive cases, although the histories were negative, found 100 per cent giving complete fixation at 8°C. with cholesterin, 92.5 per cent with this same antigen in the thermostat and the same percentage with plain antigen in the ice box. In another series of positive cases, generally treated and under treatment, the cold cholesterin fixation was 70 per cent positive in 64.1 per cent of cases. Detweiler in 300 random cases found 28.3 per cent to give a positive reaction by warm fixation with cholesterin and 22.6 per cent with cold fixation with plain antigen. All the positive cases with plain antigen were positive with cholesterin and the reactions in variance (4.7 per cent) all proved to be probable syphilitics. This writer is strongly inclined to favor cholesterin antigens but qualifies this by advising a control run with plain antigen especially as cholesterin may give complement fixation in nonsyphilitic conditions, inasmuch as fixation is especially common in pregnancy and febrile states.

The real merit of cholesterin antigen is when it makes more definite the relatively weak plain antigen fixation. Especially is this noted in early primary, neuropathic and treated cases. Nevertheless it does not follow that fixation with cholesterin will confirm all cases positive with plain antigen. Ottenberg, with 1241 cases found 2 per cent positive with plain, but negative with cholesterin antigen. My records are generally in accord with his. Its shortcomings lie in its fairly frequent spurious fixations, which, fortunately, plain antigen never brings about. A limited series (16) of tests by Smith and MacNeal, quite definitely nonsyphilitic, but suffered such conditions as acute articular rheumatism and typhus fever, are startling in results. Fifty per cent of these were positive with cholesterin antigen in the thermostat and 31.2 per cent in the ice chest, not only quite a reversal of the usual warm and cold fixation ratio, but also a striking exposition of false fixation, as all cases were also frankly negative with plain antigen. When though this series was combined with a considerably larger group of definite nonsyphilitics, although no clinical comment is made, in all 357 tests on 333 cases, the cholesterin fixation error is reduced to 2.2 per cent by high and

1.4 per cent by low temperature. In no instance did plain antigen give an indication of fixation.

One must conclude, that, without clinical corroboration, a positive reaction with cholesterin antigen and a negative reaction with plain antigen demands serologic confirmation and clinical explanation before a specific diagnosis can be accepted. On the other hand, complement fixation with plain antigen, regardless of the conduct of cholesterin antigen, spells syphilis and is the true diagnostic test. Cholesterin antigen, in its negative phase, is strong presumptive evidence of the absence of syphilis and as an index to treatment it probably enjoys its greatest field of usefulness.

#### CONCERNING HUMAN SERUM

*Human serum is best adapted for complement fixation determination when it is least anticomplementary.*

As a rule human serum receives less controlling attention than any other factor entering into the test. I refer here to the state of the individual at the time the blood is drawn and the procedure by which the serum is procured. We were originally advised to collect blood from a fasting patient, but soon lapsed into a disregard of this rather important suggestion. Chylous and highly lipoidal serums contain a certain amount of complement-absorbing possibility in the presence of antigen. There also may arise a state of serum colloids that allows it to gel at the inactivating temperature ( $54^{\circ}$  to  $56^{\circ}\text{C}$ ). While these factors are infrequent and may be slight, they nevertheless are not to be disregarded especially in a tight system or when complement is not individually adjusted. Craig and Nichols<sup>11</sup> have shown the reverse side of ingestion-serum influences in that alcohol at times renders a positive serum negative.

More important still is the proper handling of blood and serum. Every serologist can subscribe to the statement that in rather frequent instances the blood submitted for examination is either of an amount too small for any complete investigation and control or is in such state as to impeach the worker's best efforts. Like complement serum, the serum must be allowed to spontaneously separate from the clot and be free of hemoglobin and other cellular constituents that in themselves have a binding influence upon complement. It must be sterile not only for immediate test but for possible test repetitions and for the need of ample quantities of known

serums for titrations, checks and controls. Inactivated serum allows a more rapid bacterial growth than does fresh serum.

*Human serum should be recently inactivated before being tested.*

Noguchi has long championed the use of unactivated serum. He<sup>12</sup> contends that the anticomplementary elements that develop in human serum do so under the influence of thermal inactivation. In ridding a given serum of complement by heat and by shaking I have noted a greater increase in anticomplement action in the latter than by the former method.

Inactivation, 54° to 56° C. for a half hour, is in reality not a destruction of complement but a destruction of a possibility resistant complement fraction and other unknown complement absorbing elements that tend to develop in all serums. A complement once inactivated gradually regains a portion of its anticomplementary character.

Another phase of serum inactivation lies in the lipoid fixing bodies in serums of disease other than syphilis. It is rational to assume that in all toxic states various lipotropic elements develop in the blood stream and are variously affected by thermal influences. The syphilitic "antibody" is reduced by a temperature of 56° C. but not destroyed. There is some question of the consistency of this "antibody" resistance in the different types and stages of syphilis. The thermoresistance of the syphilitic "antibody" is apparently not enjoyed by other "antibodies." The earlier reports, especially when a notable tendency to working with unactivated serums existed, of positive fixation in cases of carcinoma, tuberculosis, scarlatina, nephritis, rheumatism and other conditions, probably were involved with this source of error.

*The native antishoop hemolysins present in a large proportion of human serums are negligible factors unless a loose system and warm plain antigen fixation is used.*

A variable amount of amboceptor is present in almost all human serums. Kolmer and Casselman<sup>13</sup> with 125 serums found 64 per cent to give a 100 per cent hemolysis (0.2 c.c. with complement and 1 c.c. 5 per cent sheep cell suspension), 20 per cent to give 75 per cent hemolysis, 9 per cent to give 25 per cent hemolysis and 7.5 per cent to give no hemolysis. Ottenberg and Frazier<sup>14</sup> out of 2158 serums found 21 per cent giving a complete hemolysis and 44 per cent showing an appreciable amount of amboceptor. Van Saun found 51 per



cent of serums giving a complete or a considerable amount of hemolysis. In a total of 6441 Bauer control tests I found 42.5 per cent of serums containing enough hemolysins to be of diagnostic value; 19.5 per cent of the entire number of tests showed serum to contain enough amboceptor to completely hemolyze 1 c.c. of cell suspension. In these tests warm fixation with 0.1 c.c. complement was used.

Before the introduction of cold fixation and with the use of a fixed large complement dose (0.1 c.c.), the occasional presence of a large number of amboceptor units in patient's serum, especially when augmented by the two amboceptor units used in the test, was of no small moment. Thus in the Bauer control tests\* cited by me (6441), the Wassermann was frankly negative in 1 per cent of cases and strongly positive in the Bauer control. In 5.2 per cent of cases when the Wassermann was fairly positive or doubtfully negative it was strongly positive by the Bauer. Neill,<sup>15</sup> working with positive serums to which increasing amounts of amboceptor were added found that with strongly positive serums, 0.2 and 0.1 c.c. were unaffected by the addition of 10 units of amboceptor and that a strong positive serum was never made negative. But when the serums were considerably diluted a reduction in fixation from 20 to 55 per cent with 5 amboceptor units and from 30 to 70 per cent with 10 units was noted; also that when very weakly positive serums were used fixation fell in a very appreciable degree with 5 units.

Certain methods of native hemolysin control, aside from the tests devised to utilize this factor, have been suggested. The absorption method of Rossi occasionally fails to absorb, occasionally increases the anticomplementary factor and occasionally lowers the serum "antibody" content. Kaliski defers the addition of amboceptor in the last phase of the test until the absence of hemolysis is noted.

When, however, the amount of complement entering into the test proper is just sufficient to hemolyze its quantity of cells, plus that amount necessary to satisfy those anticomplementary elements introduced with serum and antigen and when complement is definitely bound, the amboceptor factor of human serum needs no consideration. But, on the other hand, when a portion of unbound complement is available, by the law of quantitative relationship an ultimate hemolysis will occur. This free complement may be present when a loose system, containing several units of complement, is tested in

\*With the usual Wassermann set-up I ran two tubes, each receiving patient's serum and complement, one receiving antigen and neither receiving amboceptor.

fixability with a serum of low "antibody" content or when loosely bound complement, through imperfect fixation, can be detached.

As an example of the latter I present a weakly positive serum which with 2 units of complement, fixation being at 8° C. for 4 hours, showed no hemolysis with 2 or 10 units of amboceptor, but when fixed in the thermostat for 1 hour showed a 50 per cent hemolysis with 2 units of amboceptor and complete hemolysis in 10 minutes with 10 units of amboceptor.

#### TEST METHODS

Many laboratories, especially those of limited tests, still use a 2 or 3 tube Wassermann system with fixed complement, plain or cholesterinized alcoholic extract antigen and warm fixation. One alive to the broadening of the Wassermann technic brought about through serologic investigation, must conclude that such fixation tests are both incomplete and inaccurate.

*Regardless of minor details in set-up, those test methods involving the adjustment of complement to the sum of that amount absorbed by antigen and the serum to be tested and the freedom of one complete unit for the hemolytic phase of the reaction, when properly controlled and when fixation is determined with plain alcoholic extract antigen in the cold and with cholesterin-fortified antigen in the warm, are the tests of choice.*

Time, especially that taken by the pretest titrations, can be expedited by a rough calculation of the individual pig serums relative to their fitness in complement action and fixability and the presence of native amboceptors, as soon as enough serum for this purpose has formed. My custom is to bleed pigs at mid-day for the following day's test and on that afternoon note whether or not each is complementary in dose of 0.08 c.c. in presence of plain and cholesterin antigen, whether it contains native hemolysins in 0.1 c.c. and whether 0.1 c.c. is completely fixed by 0.1 c.c. of pooled positive serum with cholesterin antigen in the thermostat. These easily observed precautions are frequent savers of time and annoyance.

Most quantitative methods are patterned after that of Browning and McKenzie. These authors determined the unit of complement against 5 units of amboceptor. Three set-ups are then effected, (1) a series of tubes containing 1, 2, 3, and 4 units of complement

with the test amount of patient's serum in each tube, (2) a series of tubes containing 1, 2, 3, and 4 units of complement with the test amount of cholesterin antigen in each tube, (3) a series of tubes containing 5, 7, 10, 15, 20, 30 and 40 units of complement and the test quantities of patient's serum and antigen in each tube. To overcome the hemolytic factors of human serum an antioox system is substituted for the antisheep system. After all tubes are subjected to warmth for the fixation period sensitized cells are added. A serum that inhibits 5 more units of complement than that absorbed by serum and the serum-antigen combination, they consider positive. Ottenberg criticizes this method in that it is too exacting in the number of units fixed and considers that the delicacy of this method can be increased by using smaller multiples of complement units in the third set-up. This method at first appears cumbrous but in actual practice it is eminently simple and satisfactory. An antihuman system can be favorably adopted. This method is equally adapted to ice box fixation with plain antigen.

Most of the Browning and McKenzie modifications substitute pools of negative serum (free of hemolysins) for allowing the serum-fixing difference and determining the actual complement unit in pretest titration, which unit is adhered to in the final test. The use of more than 2 amboceptor units is optional. The objection to negative serum pools lies in the uncertain element of anticomplement increase acquired by serums after twenty-four hours regardless of the ideal conditions under which they are kept. As has been pointed out before, fresh human serum has usually an insignificant amount of anticomplement. Another objection to the pool is the liability of one excessively anticomplementary serum upsetting the entire fixation-hemolysis balance.

One of the most frequent variants is the amount of human serum placed in the anticomplement control tube. Many workers take twice the largest amount of serum used in the test. The occasion for this is to doubly safeguard against anticomplement factors supposedly inherent with human serum. Logically, however, this quantity should equalize the quantity used in the major tube inasmuch as the velocity of hemolysis is influenced more often by the increased number of hemolytic units than by the infrequent presence of anticomplement. Especially should the quantity be the same or may even be omitted, when complement is adjusted to the individual

serum. Some workers (Thomson, Boas, Thomas and Ivy and others), influenced by the Browning and McKenzie technic use the same largest serum dose in this tube but also a lesser amount of complement. Ottenberg not only adds 2 tubes to his test proper, to which are added 2 and 4 units of complement, but also an extra anticomplement control tube containing 2 full units of complement to be the controlling factor should the one unit complement-anti-complement control tube fail to show complete laking. Should this occur the main test 1 unit complement tubes are disregarded. I consider this ingenious combination of the Browning and McKenzie and the Thomas and Ivy methods as being highly satisfactory.

In the ordinary test set-up some workers use a single tube containing 0.1 c.c. patient's serum. While the commoner practice to be more quantitative from the serum standpoint, and use tubes of 0.2 and 0.1 c.c. serum, some have advised increasing and others decreasing amounts. It is obvious that with either extreme antigen must be proportionately readjusted. I have myself not seen occasion to use more than 0.2 c.c. in the test and find the smaller additional tube of 0.05 c.c. to be an unnecessary refinement.

The control of native antishoop hemolysins in human serum is pertinent to methods using a large indefinite amount of complement and with warm plain antigen fixation. With the adjustment of complement even if this be not individual, when plain antigen fixation at low temperature or cholesterol antigen fixation at high temperature is used, this factor even if present in many units is negligible.

*A Wassermann report, both for clinical and statistical reasons, should be comprehensive both in the technic used and the end reaction attained.*

A great difficulty and disappointment is met in a review of medical records relative to the Wassermann reaction. In a voluminous literature the paucity of lucid detail is appalling. This is probably engendered by the failure of the clinician to interest himself in technical details. Wassermann records, to be of any value, must conform with readily expressed and understood notations of procedure.

To the clinician a Wassermann report should be so devised that he can mentally visualize the complement-binding possibilities of a certain serum under various conditions. I have long felt the in-

adequacy and indefiniteness of the Citron (+) method of designating the degree of reaction, and this is especially emphasized by the loose application of these symbols. As the technic has broadened it has even become necessary to transcribe the ensemble of a complex reaction to a limited graphic index to satisfy the custom of the clinician.

Innovations, however, must prevail, and when determined, a report should denote the number of complement units a given serum binds. In less quantitative methods I am strongly attracted by the designating method suggested by Detweiler. He uses 3 serum tubes (0.2, 0.1 and 0.05 c.c.) and the degree of fixation with each serum quantity is given a numerical value of from 0 to 4. A serum completely deviating complement in all tubes is reported positive ~~444~~ and the shades of difference in the reaction of each tube are thus readily and clearly symbolized. ✓

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## A MORE INTENSIVE FORM OF ARSPHENAMINE THERAPY

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IT has well been said that there are now many methods of treating syphilis, but no method. In the past we have been accustomed to give our injections of arsphenamine at intervals that average one week. However, there are a number of reasons why it is desirable to make our treatment more intensive. The drug actually kills the organisms with which it comes in contact, but experimental evidence has shown that a certain amount of immunity may be gained by the treponemata. Also Schamberg says that when given intravenously the drug is almost completely eliminated in three days. The unkilld organisms may have time to reproduce before another injection is given. And lastly during these strenuous war times there are certain individuals who simply can not be kept under observation for a period of two months.

Two years ago a distinguished syphilographer, Pollitzer, advocated giving three full injections in as many days, but to me this method never seemed adapted for general work, inasmuch as it necessitated the best of judgment, much experience, and careful watching of the patient. In addition dangerous reactions may not manifest themselves in time to act as a warning. Several excellent men have followed Pollitzer's work, and repeated it and have told me of the excellent results that they have obtained in selected cases. The Advisory Council in Venereal Diseases of the Surgeon General's office has recommended the use of five-day intervals.

For the past eighteen months to a certain selected number of private patients I have been giving injections at seventy-two-hour intervals. Up to the present time I have given ninety-eight injections to twenty-two different patients, never giving less than three and several times as high as eight doses. There was not a single untoward result; while a number gave the usual reactions of nausea, vomiting, diarrhea and headache, there were no evidences

CASE	AGE	SEX	DURATION OF INFECTION	LESIONS	WASS.	PREVIOUS R.	NO. INJ.	LESIONS	WASS.
1	36	M	3 years	Retinitis	+++	8 arsphen.	3	Well	-
2	29	M	1 year	Latent	-	5 arsphen.	3	Well	-
3	33	M	3 weeks	Chancre	+++	1 arsphen.	7	Well	-
4	19	F	5 weeks	Secondary	+++	1 arsphen.	8	Well	-
5	26	F	Years	None	++	None 8 yrs.	3	Well	-
6	29	M	Years	Mucous patches	++	None 6 mos.	3	Well	-
7	29	M	Years	None	+	None 6 mos.	3		-
8	35	M	Years	None	+++	None 6 mos.	4		-
9	34	M	2 years	None	++	1 arsphen.	3		-
10	34	M	Years	C. N. S.	-	3 arsphen.	4	Better	-
11	27	M	6 months	Secondary	+++	None	8	Well	-
12	47	M	Years	C. N. S.	-	None 1 yr.	4	Better	-
13	41	F	Years	C. N. S.	+++	Mercury pills	3	Better	-
14	46	F	Years	Bones	+++	2 arsphen.	3	Well	++++
15	29	M	2 weeks	Chancre	+++	None	8	Well	+-
16	49	M	Years	Joint pains	+++	1 arsphen.	3	Well	-
17	28	M	1 month	Secondary	+++	None	7	Well	-
18	27	M	2 weeks	Chancre	?	None	5	Well	?
19	24	M	1 month	Secondary	+++	None	3	Well	?
20	24	F	3 months	Secondary	+++	1 arsphen.	5	Well	-
21	32	M	4 years	Latent	++	Mer. inj.	3	Well	-
22	45	F	Years	Latent	+	None 1 yr.	3		-

of any increased intolerance towards the drug. In no instance was albumin demonstrated in the urine although searched for by the heat and acid method in all cases. None of the cases showed any jaundice and none lost any weight. The preparation employed was an American brand of arsphenamine made by the Dermatological Research Laboratories of Philadelphia. The dose employed was 0.4 grams per 150 pounds of body weight. For such a dose 70 c.c. of distilled and double boiled water was used, and the sodium hydroxide solution was pure and fresh. All injections were given in the office and the patients allowed to go home immediately afterwards.

The clinical results were very good: every case which presented lesions cleared up very shortly. Nineteen of the patients showed positive Wassermanns: in one instance a course of three injections failed to change this finding, but in all other instances, bar one, the Wassermann became negative with great promptness: the one case in which there was no subsequent report was lost sight of.

This method has not been employed as a routine, but simply in all classes of cases which would cooperate, there was no other method of selection used. I am by no means prepared to say that it is the only method or the ideal method, but only that it is very effective, absolutely safe, time saving, and that theoretically it should be superior to the long interval method.



## A NOTE ON THE TREATMENT OF NEUROSYPHILIS

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THAT there is a lack of confidence in the constitutional treatment of syphilis, as a means of combating a syphilis which attacks the central nervous system is evident from the avidity with which intraspinal therapy was taken up in the hope that it offered something better. Sufficient time has elapsed to have given intraspinal therapy a thorough trial, and today we find the medical profession divided as to its efficacy.

It is not intended to discuss this phase of the question; on both sides are men whose extensive experience and wisdom must inspire respect for their views. One can but study and weigh these observations, concluding in his own mind as to which he will follow. The ultimate decision should be guided by hypothetically placing oneself in the position of the patient: as a medical man, with full knowledge of the consequences which may be expected from syphilis which has invaded the cerebrospinal tract, and the results to be expected from systemic or intraspinal therapy, to which treatment would you submit? Having made a choice, it is a duty to endeavor to improve that method of treatment to its greatest efficiency.

One factor which has seemed to stand against systemic treatment as a means of alleviating neurosyphilis is the apparently small amount of medication which reaches the cerebrospinal canal when administered in this way. Apparently the neuro-canal is a discrete and isolated part of the anatomy in this regard, protected against medicinal invasion, so far as the spinal fluid shows, quite as thoroughly as its thick bony wall protects against external forces. Also, the exchange of secretions is normally quite inhibited. Undoubtedly this led to the adoption of the more direct intraspinal therapy.

Recovery in infectious diseases, including syphilis, is accomplished through a process of active immunization. This property resides in the body or blood; the spinal canal can be assumed to possess no inherent quality of antibody formation. Therefore such influ-

ences must reach it from the blood,—a route presenting a formidable barrier. Witness a generalized syphilis becoming latent, of itself or with little treatment, as compared with the progressiveness of neurosyphilis, often in spite of strenuous and continued general treatment.

Further corroboration of such a view may be taken from the experiments of Flexner<sup>1</sup> in the study of the passage of neutralizing substances from the blood into cerebrospinal fluid in poliomyelitis. While reporting on poliomyelitis specifically, there is no reason why the principles regarding the immune bodies might not also be tenable regarding syphilis. Quoting: "Hence we have attempted to detect in the cerebrospinal fluid immunity principles such as exist in the blood. . . . The conclusion reached was to the effect that, while possible, it was unusual for neutralizing principles to be contained in the cerebrospinal fluid during convalescence from epidemic poliomyelitis. Incidentally, it was determined that neutralizing bodies were not produced locally."

The origin of any benefits from the Swift-Ellis treatment of cerebrospinal syphilis has been a matter of debate. It has been pointed out that the serum introduced by this method brings to the cerebrospinal canal an arsenic content far below a spirocheticidal concentration. It must be remembered, however, that this serum follows an intravenous administration of arsenic and contains the products aroused in the blood thereby. Also, that the treatment is carried on, in many cases, where that quality of the blood which had once shown a positive Wassermann test has become negative, and this quality is introduced intraspinally. Further, that cerebrospinal fluid containing the toxic products engendered by spirochetes and having no other means of escape is removed mechanically.

Another source of benefit may perhaps be attributed to the following activity—again quoting Flexner: "All sera introduced into the subarachnoid spaces act as foreign bodies, and if sterile give rise to aseptic inflammation. . . . The present inquiry has arisen from the idea that under certain circumstances immunity substances enter the cerebrospinal fluid from the blood and assist materially in the healing process. If this supposition is founded on fact, we might view the inflammatory conditions occurring in the meninges, which increase their permeability to circulating proteins otherwise

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<sup>1</sup>Jour. Exper. Med., xxv, No. 4.

excluded, as beneficial; and from this it may follow that any advantage actually shown to be derived from the intraspinal administration of normal human or horse serum may be the result not of the effects of the serum as such, but of a further increase in this permeability."

The manifestations of cerebrospinal syphilis are due more to the toxic products produced by the spirochete than to the presence of the spirochete *per se*. To the retarded entrance of immunity bodies into the cerebrospinal canal might be added that when this does take place these antibodies are not specific against those toxins which it is desired be rendered innocuous. Toxins vary with the composition of the culture media upon which they are elaborated. It is known in the production of antitoxin that variation of the culture media will produce a toxin, which while toxic of itself, will not generate an antitoxin specific for the toxin produced by the microorganism in the living host. So in syphilis, it could be assumed that the toxin elaborated in the peculiar constituents of the cerebrospinal tract differs from the toxin formed in somatic syphilis. Also that the antibodies produced against a systemic syphilis are not specific against a "nerve-derived toxin." Neither, as has been stated, does the cerebrospinal tract possess the property of generating immune bodies.

For this reason the intravenous introduction of spinal fluid is advocated: That is, it will stimulate the production by the blood of antibodies specific against the peculiar toxin which the spinal fluid contains. A positive chemotaxis toward the spinal canal will be created, carrying with it these antibodies, and their entrance into the spinal canal will be enhanced by the increased permeability of the meninges, brought about by an aseptic inflammation caused by the Swift-Ellis treatment being instituted at the same time.

The following is the method adopted: Daily inunctions of mercury are given during the entire course of the treatment. At the end of 15 days this is supplemented by weekly Swift-Ellis treatments, adding to the salvarsanized serum just before inactivation,  $\frac{1}{50}$  grain of mercury benzoate, dissolved in 1 c.c. of physiologic salt solution (Lautman method). Immediately after the serum is introduced into the spinal canal, the spinal fluid which has been withdrawn is injected intravenously.

By this method is exhibited all the advantages claimed for the intensive mercurial and salvarsan systemic treatment: the intra-

spinous introduction of mercury salts; the Swift-Ellis treatment; and those biologic advantages which might accrue from the intravenous injection of spinal fluid. This latter advantage is of course, conjectural, as there has been no opportunity to reach definite conclusions by experiment. It does, however, give promise that such investigation might be profitably conducted.

While only a small number of cases have been treated in this way, a thorough and complete laboratory study of the spinal fluid has shown that in this light at least, the results were equal to that accomplished by twice the number of Swift-Ellis or mercury benzoate treatments. For instance, comparing findings in this method with those of the previous methods, it was found that by this method three treatments gave a laboratory improvement equivalent to that of six of the other treatments mentioned.

The reactions have seemed less severe than those attending the other methods. It would be expected that adding a mercurial salt to a salvarsanized serum would increase the irritant constituents, causing a proportionately more vigorous reaction, but this has not been found true. Probably mercury and arsenic each have a selective action in the spinal canal and the combination of both is not equivalent to an increase in either salt in this regard.

Clinically, the few cases so treated, have lent encouragement to further use and observation of this method of treatment.

The intravenous injection of a spinal fluid having a four-plus Wassermann test has not been found to influence a negative blood Wassermann.

## TREATMENT OF NEUROSYPHILIS

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RECENT medical literature is filled with various methods of treatment of central nervous system lues. The advocates of intraspinal therapy are numerous and the results of many of them encouraging. But after we have followed cases consistently and with the greatest cooperation from the patient we are very apt to exclaim in despair: "Will we ever learn anything about the treatment of cerebrospinal syphilis!" Have we, after all, attained results in the intraspinal methods not attainable by the conservative treatment with mercury and salvarsan? We are depending too much in these times of laboratory methods on the laboratory diagnosis of central nervous system syphilis; perhaps we should not get too far away from the experience of Hutchinson, but should place our main reliance for diagnosis on the clinical examination. In other words, are we using the laboratory to substantiate and clarify our diagnosis, or are we depending upon a positive Wassermann, which as we know, is unreliable in the hands of inexperienced laboratory workers?

It is well then, to consider these three points: first, more careful study of the individual case to try and fit the treatment to the case; second, the value of a careful clinical examination; third, the laboratory as an aid to diagnosis, and repeated laboratory examinations in the prognosis and treatment of cases.

CASE 1.—H. M., fifty years old, complains of shooting pain in legs and swollen ankle joint. Examination shows Argyll Robertson pupil, absent knee jerks, and Charcot joint. At another clinic he had received seven intraspinal treatments. Following the last he was paralyzed in his lower extremities for several days. His condition was unimproved. In our clinic his blood was negative, and he refused spinal fluid examination. He was put on intramuscular mercury inunctions and mercury with chalk. He has improved to such extent as to leave the Relief Home and take a position at his occupation as engineer.

CASE 2.—S. A., thirty-five years old, complains of crises of gastric pain and vomiting for several years, unrelieved by food, by vomiting, or medication. Examination shows Argyll Robertson pupils, absent knee jerks, and girdle anes-

thesia. Diagnosis: tabes. Frequent examination showed absence of positive laboratory findings. He was given several intraspinal treatments with absolutely no improvement.

CASE.—F. C., forty-six years old, complains of shooting pains and burning sensations in legs. Has difficulty in walking in dark, difficulty in starting urine, occasional diplopia. Eight years ago had attacks of violent vomiting. Had seven months of mercury and K. I. Wassermann was negative, five years ago after treatment. Examination shows atrophic muscles, irregular and unequal pupils, shotty cervical glands, active reflexes, diminished sensations, slight Romberg. Blood Wassermann +, spinal fluid Wassermann +, 72 cells, Noguchi and Nonne +. Eye examination shows a double primary atrophy. He has thus far received two intraspinal injections, together with mercury rubs and K. I. His pain is greatly relieved, and he is able to work.

Of these three cases receiving intraspinal treatment, Case 3 received relief from pain and was improved, while Case 2 was unrelieved after several injections, and refused further treatment on account of the reactions. Case 1 became worse, and improved only when more conservative methods were employed.

These three cases are typical of many seen in the wards and clinics of the University Hospital. We have concluded that intravenous arsenical preparations should be employed first in all cases of nervous system lues, accompanied by intramuscular injections of mercury, either the benzoate or the salicylate, or if the patient is in the hospital, by daily inunctions. Intraspinal treatment should be given only after the conservative treatment has been employed and then only for the relief of pains of crises in tabes and cerebrospinal lues. In paresis and taboparesis death seems to have been hastened in at least two cases, although there was temporary improvement.

The following case is an eloquent appeal for more thorough physical examination, and shows how a mistake in diagnosis may lead to years of delay in proper treatment and unwarranted misery to the patient:

CASE 4.—E. M., thirty-four years old, complains of knife-like pains between the shoulder blades and in the small of the back. She has had pain and vomiting after eating, off and on, for twenty-one years. Has had eight abdominal operations to relieve the condition; for stomach ulcer, gall bladder drained, two laparotomies, gall bladder removed, adhesions broken up, gastroenterostomies, and another for postoperative adhesions. Condition unrelieved. Examination shows left pupil does not react to light, reflexes hyperactive, patches of diminished sensation on legs and thighs around lower chest. Blood Wassermann negative. Spinal fluid Wassermann negative. Noguchi negative, Nonne negative, 12 cells. Gold chloride shows a typical luetic curve. Second spinal fluid showed

53 cells. Diagnosis: cerebrospinal syphilis. She was given five injections of mercurialized serum. After the last injection the spinal fluid was negative with the exception of the gold chloride which remained positive. The pains completely disappeared. The patient was able to go about her duties and has returned home.

Cases occasionally occur, however, in which physical examination is negative. The physician should be particularly careful in inquiring into "rheumatic pains" and in investigating headaches, dizziness, visual disturbances, vomiting, difficulty in holding or starting urine, paresthesiæ, loss of memory, depression, nervousness, languor, loss of weight, fever, loss of appetite. The scalp, pupils, glands, reflexes and sensations should be carefully examined.

CASE 5.—N. K., thirty years old, complains of bad cold and headaches. Denies venereal disease. About three months before coming to the clinic he contracted a cold, grew weak, and had to give up work. Has lost 18 pounds of weight in three months. Physical examination negative. Blood Wassermann +++. Spinal fluid 12 cells. Noguchi and Nonne ++, gold chloride luetic curve. He was given two salvarsans and his headaches completely disappeared. Further treatment consisted of four intravenous bichlorides, mercury rubs and K. I. for a short time. The patient did not return.

CASE 6.—H. L., thirty-three years old, complains of headache and a primary two years ago. Treated by a physician who gave one salvarsan and mixed mercury and K. I. In three months had considerable headache and dizziness. Examination negative, except Achilles reflex not elicited on one side. Blood Wassermann ++, spinal fluid Wassermann +++, 560 cells, Noguchi and Nonne ++. Gold chloride luetic curve. Diagnosis: syphilitic meningitis. He received six salvarsans at intervals of a week. The cell count was reduced to 23, Nonne and Noguchi negative. The headaches were completely relieved. The patient was advised to continue treatment with inunctions and to return in three months for further observation and treatment.

In a case seen recently, similar to Case 6, the absence of an Achilles reflex on one side, all other physical findings being absolutely negative, led to the examination of the spinal fluid and the discovery of a triple positive Wassermann.

In a recent report on two hundred cases of lues, by the Clinical Society of St. Luke's Hospital in San Francisco, it was concluded that a careful clinical examination is of more value than a study of the Wassermann reaction; that in one hundred cases of syphilis clinically positive, twenty gave a negative Wassermann. These cases, however, were of all types of syphilis. In syphilis of the central nervous system we have found the Wassermann test a most valuable adjunct, but we place most reliance on the clinical findings.

The value of frequent laboratory examinations and especially the gold chloride reaction can not be emphasized too strongly. The gold chloride test requires a very small amount of spinal fluid and is of a definite diagnostic and prognostic value. In a recent investigation of 100 cases in the clinic and hospital the gold chloride reaction was positive in 100 per cent of paretics and in 90 per cent of tabetics, and negative in 100 per cent of negative cases. In our clinic three cases of cerebrospinal lues without marked mental symptoms were prognosed unfavorably on the gold chloride alone, and recent developments have justified our reliance on the spinal fluid findings, each of the three cases having developed a paresis.

CASE 7.—E. M., thirty-eight years old. Complaint: difficulty in urination. Family history negative. Past history: at sea for ten years. About 15 years ago, rheumatism in shoulders, hips and knees. Genital sores 18 years ago. Treated by ship's doctor. Present history: for several years has had difficulty in starting urine; last two years more severe. Retention for 18 to 24 hours. No incontinence. Sexual power impaired; attributes it mostly to worry. Referred to the nerve clinic. Blood +++. Spinal fluid increased pressure. Spinal fluid Wassermann +++, 23 cells, Noguchi and Nonne positive, gold chloride 5455432200, paretic curve. Patient thinks he is losing his memory. Feels very much depressed over his condition. Has pains in back of head and neck and back of legs. For the past three weeks has had difficulty in speech. Mental examination: Orientation good; no difficulty with test phrases. Patient says he had an attack of aphasia, lasting a few minutes. Memory: Remembers street numbers for twenty minutes. Reading: O. K. Writing: Has difficulty because of tremor. Has no delusions or hallucinations. Invested in a jitney bus and lost his money. Is afraid his boss's business will fall through and he will lose money owed him. Says he feels sleepy all the time. Goes to sleep if he sits down. Later examination shows marked tremor of the lip, extreme nervousness. Worries a great deal. Memory is failing. Has shooting pains in his head. Examination by the psychiatrist resulted in a diagnosis of general paresis. Received treatments of K. I. 32 intramuscular injections, 10 intravenous injections of bichloride of mercury. The case shows how the gold chloride test may assist us in anticipating later developments.

CASE 8.—I. M., forty years old. Family history negative. Past history: Chancre in 1904. No symptoms. Internal medication started immediately and continued for ten months. No salvarsan. Since then has used three or four bottles of mixed preparation. He thinks he has noticed symptoms of locomotor ataxia. Has read a great deal about syphilis. Has recently had severe headaches and diplopia. Is very sensitive to hot and cold water. Tires readily. Can not run. Has pin and needle sensations in legs. Shooting pains in legs. No incontinence but difficulty in starting urine. No girdle sensation. Is greatly worried about family and finances. Very irritable, memory poor. Physical examination: right pupil is larger than the left; reacts sluggishly to light. Ab-



dominal reflexes active. Knee and ankle jerks not obtained. Back extremely hyperesthetic to cold and pin. Diminished sensation to pin in outside of left leg. Blood +++. Spinal fluid Wassermann +++, 52 cells, Noguchi and Nonne ++. Gold chloride, 1555555310. Examination by psychiatrist led to a diagnosis of possible beginning paresis or psychogenic depression due to physical condition. Has been treated very irregularly. In six months has had 26 intramuscular injections. For a while felt quieter in his nerves, but at the last visit felt dizzy and reported two petit mal attacks. Has had frequent periods of depression. Thinks he may become a great opera singer; has learned the score of Aida in a day and says he has an extremely good voice. Diagnosis: general paresis.

We have found in a number of instances that we have been delinquent in not pushing treatment more vigorously and thoroughly. The following case illustrates the clinical improvement which may follow treatment, while on the other hand, laboratory tests reveal a steadily progressive disease process.

CASE 9.—H. A., twenty-five years old, came to the throat clinic in 1915, complaining of pain in the throat and hoarseness. Examination showed tonsils covered with gray-green crusts. Wassermann +++. Family history negative. Past history: denies venereal disease. Present history: About six weeks ago noticed that his throat was sore, until one week ago, when he received an injection of salvarsan. Since then it has cleared up. About three weeks ago a rash broke out, first on his face and hands and then on his body. Now it has cleared up. Examination: Pupils are equal, regular, and react to light and distance. Tonsils ulcerated. Few palpable cervical glands. The remainder of the examination was negative. Temperature 100.1°. Received 15 intramuscular injections. Weight increased eight pounds. Two weeks later was hit on the head by a ball just over the left eye, not unconscious. Two days later had nose-bleed; then bad headache; nauseated and vomited later, suddenly fainted. No trouble with vision. X-ray of skull taken and was negative. Lumbar puncture: Wassermann negative. One month later memory badly impaired. Did not remember his letters. Could not write a sentence except with great difficulty. Very dizzy and vomited. Had occipital headaches. One month later could not read his music. Had severe continuous headache. Put on mercury and chalk and K. I. Psychiatric examination showed an alexia and agraphia. For one year was treated twice a week with mercury injections and K. I. Blood Wassermann was negative. The spinal fluid, however, showed 671 cells. Nonne and Noguchi ++. Wassermann +++. Was given three old salvarsans .3. Spinal fluid 51 cells, Noguchi and Nonne negative, Wassermann anticomplementary. Received four intravenous salvarsans. Spinal fluid 13 cells, Nonne and Noguchi positive, luetic colloidal gold curve, Wassermann positive in 0.3. Received ten intramuscular injections. The patient is clinically greatly improved, has no dizziness or headache, and follows his profession of musician. Without a spinal fluid examination, however, and a more vigorous treatment intravenously, the result would have undoubtedly been exceedingly discouraging.

CASE 10.—J. M., seven years old, underweight and complaining of chronic cold, was seen in the hospital. Examination showed unequal pupils, one of them not reacting to light, active reflexes, blood +++. Spinal fluid Wassermann +++, high cell count and + globulin. The gold chloride and mastic showed a paretic curve. Mother's blood ++. Diagnosis: Juvenile paresis and congenital lues. About ten salvarsans of adult dosage were administered at intervals of a week and the spinal fluid repeatedly examined. The Wassermann and cell count gradually became negative, but the mastic and gold chloride remained positive for paresis. There is no clinical improvement. The prognosis is unfavorable clinically and by the laboratory tests.

A negative Wassermann in the blood serum should not rule out syphilis. Faint positive and single positive Wassermans are of little value without definite clinical findings. Effects of previous treatment on serologic and spinal fluid tests should be borne in mind. There is usually no justification for a spinal puncture without positive clinical signs. Cell counts in the spinal fluid are of the greatest positive value. After an examination of hundreds of fluids I have come to the conclusion that cell counts mean more than the Wassermann and are at least as valuable as the gold chloride reaction in diagnosis. Three cells per c.mm. should be taken as the minimal count. During treatment a reduction in the cell count occurs before the Wassermann diminishes. In reporting the spinal fluid Wassermann, the physician should insist on the amount of fluid used in performing the test as the Wassermann may be + in 1 c.c. and negative in 0.2. The antigens used in the Wassermann test should be specified. A cholesterinized reinforced antigen and a simple antigen should be used with each specimen. In the University Hospital we use a cholesterinized and two simple antigens.

#### CONCLUSION

Intravenous arsenical treatment in central nervous system syphilis should be employed, together with mercury, before resorting to intraspinal methods, which should be used only for the relief of pain and crises.

A careful clinical examination should form the basis for diagnosis of lues of the central nervous system.

The Wassermann test should be employed as an adjunct to the clinical examination. In diagnosis, the spinal fluid cell count and the gold chloride test confirm the Wassermann. The gold chloride curve is of great value in prognosis.

# Abstract of Current Syphilis Literature

It is the purpose of this JOURNAL to review so far as possible all literature on syphilis as it appears in other medical periodicals and to present it in abstract form. Authors are requested to send abstracts or reprints of their papers to the Associate Editor, Dr. Wm. H. Deaderick, Dugan-Stuart Bldg., Hot Springs, Arkansas.

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WM. H. DEADERICK, M.D., EDITOR

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PAPULAR AND NODULAR FORMS OF CHANCROID IN THE BALANOPREPUTIAL REGION.—Ferrand (Tremblay. *Presse médicale*, 1918, vol. xxvi, p. 375.

The diagnosis of chancroid is made usually by its general appearance, brief incubation period, character of adenopathy and results of autoinoculation. It represents essentially a loss of substance, being a necrotizing ulcer, surrounded by a sensitive inflammatory zone. A typical form occurs in which these characters are absent. One such is the elevated papule, which violates the rule of a loss of substance. The other has a distinctly nodular base. Both these forms are readily confused with chancre. Especially is there likelihood of the diagnosis of mixed chancre in the nodular form. These atypical chancroids tend to occur in certain localities, as the balanopreputial fold and free margin of the prepuce. In the author's experience, about one chancroid in ten is atypical. It must not be inferred that these formations are really difficult of diagnosis by an expert for the presence of the bacillus of Ducrey will of course make the diagnosis of chancroid and we also have the short incubation, etc. To exclude syphilis straightway may not be so easy a matter but in certain cases a biopsy is possible with demonstration of the spirochetes, and a repeated negative Wassermann will exclude syphilis. A positive Wassermann could mean chancroid with antecedent syphilis. The author is a pupil of Darier, whose histologic criteria of suspicious lesions are used to check up the finds of serodiagnosis. Nevertheless he believes in a thorough clinical expertisation of these lesions. The elevated papule comes about because of an excessive production of granulation tissue analogous to proud flesh in ordinary streptococcus ulcers. This vegetating tissue may transcend the original area of the ulcer. The papule remains stationary for a considerable period and may be single or occur in large numbers, in either case resembling secondary syphilitic flat

papules. Ordinary chancreoids may coexist. In the nodular form there is no true induration such as occurs in the Hunterian chancre. It looks like a chancre but does not feel like one. It is sometimes difficult to palpate it properly. The history shows that the lesion was at first a typical chancreoid in which the nodular base appeared as a later development. The mixed chancre has a similar evolution.

A CASE OF SYPHILITIC REINFECTION.—Joseph Spangenthal, Buffalo. *Journal of the American Medical Association*, 1918, vol. lxxi, p. 730.

Several weeks after the patient's infection, the wife presented a secondary papular syphilide, angina, and mucous patches. The chancre involved the whole cervix uteri. About a month later she developed an optic neuritis, with complete blindness of one eye. This cleared promptly after an intravenous injection of neoarsphenamine (neosalvarsan). October 2, 1913, the man was given 0.9 gm. of neoarsphenamine (neosalvarsan) intravenously. October 18, this treatment was repeated. October 26, intramuscular injection of mercuric salicylate 1 grain in oil, was administered, and repeated weekly until four injections were given. This constituted the entire treatment. Every six months the patient reported for a Wassermann test, which in every instance gave a negative reaction. In March, 1918, the patient was in Boston, and while there a Wassermann test was made, and reported negative. During March, he gives a history of frequent and prolonged kissing. The girl in question was at time suffering from syphilis, and had later received four injections of arsphenamine (arsenobenzol). About April 1, 1918, the patient developed a chancre of the upper lip. May 14, he again consulted the author. The chancre was still present, but undergoing resolution. There was a secondary maculopapular eruption covering the entire body, accompanied by angina and glandular involvement. There was no mistaking the clinical picture of syphilitic infection. In order to satisfy the patient as to diagnosis, a Wassermann was made independently by two serologists, and both reports were + + +, showing complete inhibition of hemolysis.

ANNULAR MACULAR SYPHILIS.—John J. Rothwell, New York. *Journal of Cutaneous Diseases*, 1918, vol. xxxvi, p. 397.

So clearly definite a picture of erythema multiforme (except for the presence of the two pea-sized papules) was presented that a diagnosis from objective symptoms alone might easily have been incorrect. One is prompted to suggest the advisability of a Wassermann examination in a case of supposed persistent erythema multiforme, especially in the female, genital lesions in this sex so often escaping observation. Another point worthy of recollection is that there was a rapid disappearance of the eruption under usual treatment as opposed to the

usual belief that the annular macular syphilide may be resistant to treatment. No spirochete examination was made, the indurated genital lesion, the adenopathy, and the eruption with its two very suspicious papules making a diagnostic picture, amply sufficient to warrant the institution of antisiphilitic treatment for the sake of gaining time in getting the disease under control, until the Wassermann report (one week later) should be known. The Wassermann proved to be ----, and the patient responded rapidly to treatment.

**PERFORATING ULCER OF THE HARD PALATE RESEMBLING TERTIARY SYPHILIS.**—Lewellys F. Barker and Sydney R. Miller. Baltimore, Md. *Journal of the American Medical Association*, 1918, vol. lxxi, p. 796.

Vincent's disease is in all likelihood a primary periodontal gingivitis, occurring frequently in certain particular areas, liable to develop anywhere in ill-kept mouths, associated with characteristic gum lesions, and capable of spreading to any part of the buccal cavity or throat. The disease is both infectious and contagious. The lesions most often seen clinically are ulcerations of the tonsils, to which the name "Vincent's angina" should be restricted. No matter where located, the lesions of Vincent's disease are caused by the activities of the *B. fusiformis* and an associated spirochete. Their specificity is as yet unsettled. It is quite likely that they normally are symbiotic saprophytes, capable under certain conditions of causing pathologic changes. The diagnosis of Vincent's disease from syphilis is simple. Smears from the lesions usually suffice.

Cases of uncomplicated Vincent's disease invariably give a negative Wassermann reaction. The local application of concentrated solution of arsphenamine is regarded as the best form of therapy. Most cases clear up within a few days. Prophylaxis is better than cure. Oral sepsis is inexcusable.

**MALIGNANT SYPHILIS OF THE UTERUS.**—George Gellhorn. St. Louis, Mo. *Interstate Medical Journal*, 1918, vol. xxv, p. 515.

In this young colored girl of 17 years, a syphilitic infection ran its entire course from the initial stage to a fatal ending in less than a year. The diagnosis was secured by the findings of spirochetes in the secretion and in the tissues of an extensive secondary ulceration of the cervix. A point of unusual interest was the symbiosis of spirochetes and gonococci in the tissues of the ulcer. Within two months this ulceration had changed into a large cauliflower tumor which, histologically, presented a clear-cut picture of gumma. In this stage the Wassermann test was negative, obviously due to the fact that the marked and rapidly progressing cachexia of the patient prevented the formation of antibodies in the blood. Antisiphilitic treatment was of no avail, and the patient died of a perforative

peritonitis from a retroperitoneal abscess between uterus and sacrum. This abscess, primarily, was in all probability a gumma which had extended from the cervix through the parametrium into the pelvic cellular tissue and had arrodged large portions of the pelvic bones. Secondly, microbes invaded this gummatous infiltration from the necrotic surface of the cervical tumor and brought about an abscess which eventually broke into the abdominal cavity. Finally, the findings at autopsy of a gumma in one of the ovaries should be recorded because of its excessive rarity. The rapidity and intensity of the syphilitic process in this case was, perhaps, due to a particularly virulent strain of spirochete, aided and abetted by a racial lack of resistance, as it is well known that in negroes syphilis assumes more severe forms than in white patients.

**SYPHILIS OF THE BLADDER.**—Fred H. Cole, Detroit, Michigan. *The Urologic and Cutaneous Review*, 1918, vol. xxii, p. 482.

Syphilis of the bladder is much more common than formerly suspected and is frequently overlooked. While the "roseola" is pathognomonic, the several pathologic lesions, especially ulcers of the bladder without bacteriologic findings, should be viewed with suspicion. Cystoscopy is one of the most valuable adjuncts in diagnosis. The possibility of an infected bladder and syphilis, with an improvement of bladder symptoms following treatment of the syphilis, is to be thought of. The result of treatment is the most positive evidence in diagnosis. Suspected and treated, the prognosis in bladder syphilis is good.

**CONGENITAL SYPHILIS OF THE KIDNEY.** A. F. Canelli. *La Pediatria*, May 1918.

Congenital syphilis of the kidneys is found to be rather frequent on autopsy. It is shown by presence of sclerotic atrophy, gummata and cysts from retention. Amyloid degeneration of kidneys is not characteristic of syphilis in its congenital form. There may be acute interstitial nephritis, or a chronic sclerous atrophic form. Tardy inherited syphilis is frequently manifested by a syphilitic albuminuria.

**SYPHILITIC JOINTS.**—Perey Willard Roberts, New York. *New York Medical Journal*, 1918, vol. cviii, p. 108.

It should not be assumed that every patient enjoys a prompt and rapid recovery. Results will vary according to the type of tissue invaded, the virulence of the organism, and the co-operation in treatment which the patient is willing to give. Where there is no bone involvement joint symptoms of long standing usually disappear in a few weeks, and sometimes with astonishing rapidity. Bone lesions,

on the other hand, clear up slowly, even when the accompanying acute symptoms subside quickly. Where regeneration of bone does take place approximately, a year or more of continual treatment is necessary.

OBSERVATIONS ON OCULAR SYPHILIS.—Jesse H. Simpson, Louisville, Kentucky. *The Urologic and Cutaneous Review*, 1918, vol. xxii, p. 388.

Contrary to ideas formerly prevailing, interstitial keratitis may occur during the course of acquired syphilis, numerous typical examples having been recorded. Scleritis and episcleritis may be observed as early or late manifestations. Iritis is one of the most frequent ocular lesions due to acquired syphilis. In type it may be either serous or plastic; and its development may be early (iritis pululosa) or late (iritis gummosa). The iris becomes congested, nodular and thickened; ciliary injection is usually marked; exudation occurs into the anterior chamber; synechiae often follow the plastic type. Cyclitis usually occurs in association with iritis (iridocyclitis), but may develop independently. Choroiditis is a common luetic manifestation which may occur alone or with retinitis. Retinitis may develop independently or as an extension from the choroid. In type it may be simple, exudative or hemorrhagic. Optic neuritis may be an essential luetic sign. It has been claimed that in over 50 per cent of instances paralysis of the external ocular muscles may be correctly attributed to syphilis. Whether this observation is correct or otherwise the author is unable to positively state; but the estimate seems reasonable when it is remembered that ocular paralysis is usually among the later manifestations of the disease. Tarsitis of syphilitic origin has been described as a late manifestation. It is usually bilateral and develops gradually without appreciable pain. The osseous structures of the orbit, and likewise the lacrimal apparatus, are sometimes involved during the later stages of acquired syphilis.

INTERESTING CASE OF A FACIAL PARALYSIS IN A SYPHILITIC.—Fernando Sanz, Madrid. *El Siglo Medico*, 1918, vol. lxx, p. 522.

The patient was a man of 46 years of age, married and of good social status, who four years before had suffered from a stroke of hemiplegia with resulting aphasia. It was apparent that his misfortune had been due to syphilitic disease of the cerebral arteries. Under appropriate treatment he had secured much benefit without the development of any new accident. The aphasia vanished and the asymmetry of the facial innervation had been restored. In the limbs recovery was much less in evidence and he presented a classical picture of spastic hemiplegia. His treatment went ahead, both

specific and physical, and incidentally he had been badly salivated on several occasions as a result of bad mouth hygiene. These attacks interfered with the original plan of treatment. During a fresh course of injections of grey oil he was suddenly seized with left facial paralysis. In the belief that the patient had had a second stroke the author was called in consultation. The diagnosis was peripheral facial paralysis due probably to a gummous meningitis of the base of the brain involving the facial nerve. But further investigation showed the possibility of another origin. The mercurial stomatitis had evidently given rise to a parotitis with possible mechanical compression of the nerve trunk. The likelihood prevented the author from pushing the mercury to greater lengths, which he would have done in meningeal syphilis. The Wassermann was now found to be negative and on the suspension of the mercury the paralysis cleared up.

**OBLITERATING ARTERITIS WITH GANGRENE OF THE FEET IN SUCCESSIVE ATTACKS. SEGMENTARY ENDOPHLEBITIS AND PERIPHLEBITIS OF THE LIMBS.**—Gougerot and Clara. *Annales des Maladies Vénériennes*, 1918, vol. xiii, p. 389.

A case reported in great detail of a man of 27 years who after premonitory symptoms was attacked by subacute arteritis of the left foot. In about a week's time the obliteration of the vessel was indicated by the supervention of gangrene of the great toe, which was amputated. A second crisis of the same sort led to resection of the first metatarsal bone and for several years past the left foot has been spared further attacks. The right foot, however, was attacked nearly two years after its fellow, and in a similar manner. The toes did not suffer, but gangrenous areas appeared in the dorsum of the foot. Successive attacks then made it necessary to amputate in the lower third of the leg. It was learned that the veins had suffered with the arteries during these crises, chiefly with periphlebitis. The fact that this recurrent arteritis is practically always syphilitic led the authors to report the case in the *Annales*. It was, however, impossible to prove the existence of syphilis in this patient, for 3 Wassermans taken in succession were negative even after attempts to reactivate it. Anti-syphilitic treatment was negative, there was no stigmata, no historical data, pointing to the disease. It was equally impossible to connect the lesions with tuberculosis or streptococcemia. The exciting cause was doubtless exposure to cold.

**THERMOLABILITY OF SO-CALLED SYPHILITIC ANTIBODY.**—E. H. Ruediger, Bismarck, North Dakota. *Journal of Infectious Diseases*, 1918, vol. xxiii, p. 108.

Unheated serum frequently gives a much stronger positive result with the Wassermann test than does heated serum. The use of un-



heated serum is not practicable because it must be tested while still fresh, and because the complement present would interfere if one wished to use large quantities of serum. In quantities of 0.5 c.c. of unheated human serum per test tube the native complement was not perceptible in the tests. Quantities of 0.125 c.c. of heated, glycerolated serum per test tube gave stronger positive results than did quantities of 0.005 c.c. of unheated serum. Heated glycerolated serum gave a little stronger positive results than did heated nonglycerolated serum.

**OPHTHALMIC CHANGES IN TABES AND PARESIS; THEIR RECENT PATHOLOGY AND DIAGNOSIS, PARTICULARLY WITH REFERENCE TO CEREBROSPINAL SYPHILIS.**—Israel S. Wechsler, New York City. *New York State Journal of Medicine*, 1918, vol. xviii, p. 312.

From the study of the more recent investigations of the pathology of neurosyphilis, particularly with reference to optic changes, the writer has gained the impression that there is no fundamental difference between tabetic neurosyphilis and so-called cerebrospinal or, better, diffuse neurosyphilis. It seems evident that an inflammatory process is behind every form of syphilitic involvement and that the spirochete is at the bottom of the reaction. Obviously, the inflammatory reaction is in direct proportion to the kind of tissue involved. There is every reason why the meninges should respond more violently than the parenchyma of the brain. The reaction, too, of the vascular, interstitial structures will be of a different nature than that of parenchymatous tissue. But lymph and plasma cell infiltration and mast cells are the fundamental characteristics of syphilis.

This picture occurs in tabes, paresis and optic atrophy, just as it does in interstitial neurosyphilis or, say, aortitis. There is, therefore, no valid reason for calling a protean clinical picture cerebrospinal syphilis. In the first place, tabes and paresis are anatomically just as cerebral and spinal, and secondly, the pathology is based in all cases on a similar reaction to the same agent. I have, therefore, without being too consistent, used the term interstitial, or diffuse neurosyphilis, instead of cerebrospinal lues. The same argument, it seems, holds true when we come to the pathology of special structures, such as the optic nerve. Evidently very careful examination has revealed inflammatory reactions, even in very old cases of optic atrophy. It would seem advisable therefore to drop the term primary optic atrophy or, rather, employ it in the sense that the atrophy takes place *pari passu* with the inflammatory, exudative process. It is equally descending with an inflammatory neuritis, though the vascular changes are not nearly so violent. The deductions to be drawn are quite obvious. Without attempting to deal with the subject of therapy it may be well to point out that if the inflammatory character of optic atrophy will come to be recognized, we may be able to at-

tempt rational and possibly hopeful treatment in cases which have hitherto been the despair of therapeutics.

INTERPRETATION OF NEGATIVE LABORATORY FINDINGS IN SYPHILIS.—

Albert E. Sterne, Indianapolis, Indiana. *Journal of the American Medical Association*, 1918, vol. lxxi, p. 89.

A positive Wassermann reaction of blood, and especially of spinal fluid, spells syphilis and syphilis only. A negative serum Wassermann reaction and even a negative spinal fluid Wassermann reaction does not strictly indicate the absence of syphilis. Laboratory tests are merely clinical signs, which at times may be present or absent, like other symptoms; spinal fluid tests should always be made together with blood serum tests. Correct interpretation can be made only by weighing carefully the clinical evidence, with the serologic reports, especially when the latter are negative. This can not be too emphatically emphasized. Laboratorian and clinician should hold far closer scientific relationship than is now usual. They should be mutually helpful. The laboratory findings should fit into the clinical syndrome and not vice versa. And unless there is wise, deliberate interpretation of laboratory data, especially negative data, in neurologic and other cases, serious errors in diagnosis and treatment will continue.

A STUDY OF FOUR HUNDRED POSTMORTEM WASSERMANN REACTIONS.—

Stuart Graves, Louisville, Ky. *Journal of the American Medical Association*, 1918, vol. lxx, p. 1753.

Postmortem reactions confirmed antemortem Wassermann reactions in 97 per cent, of sixty-eight controlled cases. A + + + positive reaction sixty hours postmortem, was confirmed by a + + + + antemortem in a case with anatomic and clinical evidence of syphilis. A negative Wassermann reaction on blood taken twenty-two hours postmortem was confirmed by a negative antemortem Wassermann reaction. In 91.2 per cent of cases showing anatomic lesions of syphilis and presenting evidence of syphilis in their histories, the serum postmortem gave positive Wassermann reactions. The fact that only 2.5 per cent of the serums were anticomplementary or otherwise unfit for use compares favorably with 1.14 per cent similarly unfit in 6,000 antemortem specimens. Only 2.6 per cent of 378 cases showing anatomic evidence of syphilis gave negative Wassermann reactions. The reactions conformed to the anatomic and historic evidence in 304 of 378 cases, or 80.4 per cent, which is considerably lower than it would be if satisfactory histories and physical examinations were recorded in Class 5.

There is no logical reason for supposing that acute infections or malignant tumors cause positive Wassermann reactions. The positive reaction appeared in 2.7 times as many negroes as whites, in 1.7

times as many males as females, and in only eleven white females, or 6.5 per cent. The Wassermann reaction, made on postmortem blood according to the methods followed in this investigation, is practically as reliable a test for syphilis as when done antemortem, and is of great value in pathologic anatomy and in medicolegal cases.

**A NOTE OF THE LOSS OF COMPLEMENTING POWER IN KEPT SERUM.—**

J. S. C. Douglas and J. W. Bigger, University of Sheffield. *Lancet*, London, 1918, vol. ii, p. 45.

A satisfactory method of estimating decreases in the complementing powers of sera over considerable periods of time has been devised. While kept normal guinea pig serum loses its complementing power more rapidly in the early stages than the later, and at 20 degrees C. than at 9 degrees C., yet it retains its activity for a considerably longer time than has generally been conceded. The loss of complementing power of such serum is perfectly regular and can be expressed by the formula— $dx/dt \cdot 1/x^{n+1} = K$ , at 9° C., and apparently also at 20° C.

**THE INFLUENCE OF INCUBATION ON THE WASSERMANN REACTION.—E.**

H. Ruediger, Bismarck, North Dakota. *Journal of Infectious Diseases*, 1918, vol. xxiii, p. 182.

Complement binding is better in the incubator at a temperature of 37° C. than in the open water-bath at the same temperature. It takes place gradually, many hours being required for its completion and is much better at a temperature of 10° C. than at a temperature of 37° C. or of 21° C. Perhaps the optimum temperature for complement binding and the length of time necessary for its completion in the Wassermann reaction have not been determined.

**INFLUENCE OF TEMPERATURE UPON THE VELOCITY OF THE COMPLEMENT FIXATION REACTION IN SYPHILIS.—**

Hideyo Noguchi, Rockefeller Institute of Medical Research. *Journal of Experimental Medicine*, 1918, vol. xxviii, p. 302.

Examination of syphilitic serum or cerebrospinal fluid can be made at any temperature between 23° and 37 C. The velocity of the fixation reaction, including the fixation of complement and subsequent hemolysis, is greater at a higher temperature, the optimum point being 37° C. The maximum reaction is also reached, however, when the mixture of lipoids, syphilitic serum, and complement is allowed to stand for a long enough period at a lower temperature, the minimum thermal point being near 23° C. For the optimum temperature (37° C.) an incubation of 30 minutes is sufficient, while for the minimum temperature (23° C.) 2 hours are necessary. At the temperature of 30°

C. the reaction proceeds with moderate velocity and is complete within 60 minutes. Guinea pig complement gave a sharper reaction with the sera which contained less than one unit of the fixing substance. Fixation is complete, however, at any of the three temperatures within 20 minutes when there are more than two units present. A serum containing one unit of fixing substance will complete reaction within 30 minutes at 37° C., 60 minutes at 30° C., and 2 hours at 23° C., irrespective of whether human or guinea pig complement is used. For many reasons a properly adjusted thermostat for 37° C. is recommended for conducting the serum diagnosis of syphilis when possible, but it should not be overlooked that at a temperature near 30° C. an entirely reliable result can be obtained without a special incubator. Even at a temperature as low as 23° C. the test can be carried out if sufficient length of time is allowed. The foregoing conclusions refer only to the systems in which the acetone-insoluble fraction of tissue lipoids is used as antigen.

CONCERNING BRUCK'S NITRIC ACID REACTION WITH SERUM AND CEREBROSPINAL FLUID IN SYPHILIS.—Ikuzo Toyama and John A. Kolmer, Philadelphia, Pa. *Journal of Cutaneous Diseases*, 1918; vol. xxxvi, p. 434.

Wassermann and Bruck tests with ninety-four serums (the Bruck tests being conducted with fresh active serums) yielded similar results with sixty-five serums, or 70 per cent. All of the positive reactions with both tests occurred with the serums of persons manifesting the lesions of the secondary and tertiary stages of syphilis and undergoing treatment with arsphenamine (arsenobenzol of the Dermatological Research Laboratories). With the serum of twenty-three persons, or about 25 per cent, the Wassermann tests were negative and the Bruck test positive; eight of these serums were from persons regarded as nonsyphilitic and the rest (fifteen) from persons in the secondary and tertiary stages of syphilis undergoing vigorous treatment with arsphenamine and yielding positive Wassermann reactions on admission to the clinic and prior to the time when the Bruck tests were made. According to the results, therefore, the Bruck test was found to yield presumably about 8 per cent falsely positive reactions; also that the property of syphilitic serum responsible for the Bruck test probably under treatment for a longer period than the reagin or Wassermann antibody. With the serum of six persons, or about 6 per cent, the Wassermann tests were positive and the Bruck tests were regarded as negative; all of these serums were from persons presenting the lesions of the secondary and tertiary stages of syphilis on entering the clinic and undergoing active treatment with arsphenamine. The results of Bruck tests conducted with eighty-nine serums in the fresh active state and again after inactivation (heating) showed similar results in 85 per cent; in 13 per cent the reactions were positive

with active and negative with inactive serum; all serums were from cases of secondary and tertiary syphilis undergoing treatment. It would appear, therefore, that active serum is better adapted for the Bruck test than inactivated serum. Preliminary and final readings of the Bruck test agreed in 94 per cent of serums; with 6 per cent of serums the reaction was read as positive in the preliminary and negative in the final reading. These serums were from persons in the secondary stage of syphilis and undergoing vigorous treatment; it would appear, therefore, that the precipitate yielding a positive result in the preliminary reading may dissolve overnight and thereby render a negative result in the final reading. For this reason the preliminary reading is considered more delicate but more difficult to interpret and differentiate from the opalescent reactions sometimes yielded by normal serum. Bruck tests conducted with cerebrospinal fluids in amounts ranging from 0.5 to 2 c.c. were invariably negative irrespective of the source of fluid as from normal persons or those suffering with syphilis of the central nervous system and suppurative meningitis; owing to the relatively small amount employed, and from inflamed meninges, as compared with serum, the Brock test is worthless as an aid in diagnosis. While the Bruck serochemical tests is very simple, of great interest theoretically and probably of more value than the numerous other physicochemical tests of Porges and Meier, Klausner, Herman and Perutz, and others, the reactions are less well defined and more difficult to read and more prone to error on the personal equation than the Wassermann reaction and, likewise, probably less delicate and valuable as a diagnostic reaction than the Wassermann test when the latter is properly conducted by experienced persons.

**THE RESULTS AND INTERPRETATION OF THE WASSERMANN TEST.**—Clarence A. Johnson, Los Angeles, Cal. *Medical Record*, 1918, vol. xciv, p. 62.

The time of the appearance of the syphilitic antibody in the serum after the infection varying from five days to several weeks, it must be borne in mind that a negative result may mislead the physician as to diagnosis and that a microscopic examination should be made if available. The second factor which influences the test is the amount of complement-inhibiting substance in the serum and the lesion may be fairly characteristic and give a negative reaction when it may be of a specific nature, therefore, to give the patient the benefit of this reaction another test should be made in the days following. If alcohol influences this test as has been demonstrated, the history of having taken alcohol twenty-four hours before the test should be ascertained and if taken within this time advise the patient to return twelve hours later, in order to prevent the influence of the drug upon the reaction. If the growth of bacteria influences the negative to positive, then it is abso-

lutely essential to have all needles and glassware bacteriologically clean. Since we have a method in the provocative test for bringing out such latent antibodies as may be present, this therapeutic agent should be used both from a diagnostic and treatment standpoint.

FURTHER STUDIES ON THE PRESERVATION OF COMPLEMENT BY SODIUM ACETATE.—B. W. Rhamy, Fort Omaha, Neb. *Journal of the American Medical Association*, 1918, vol. lxx, p. 2001.

For the preservation of complement the author has found that sodium acetate is ideal. It has the following properties:

- (a) It has no hemolytic action.
- (b) It is not anticomplementary.
- (c) The solution can be sterilized.
- (d) Dissolved in physiologic sodium chloride solution, it has the same hydrogen-ion concentration as blood PH7. 4.
- (e) It preserves and stabilizes complement from two to three months in the ice box, or two weeks at room temperature.
- (f) It can be used in any strength from 5 to 50 per cent or in crystal form.
- (g) Its preservative properties are not antibacterial, and therefore must be physicochemical.
- (h) Added to whole blood in certain strengths, it prevents coagulation.
- (i) It will preserve human complement.

A PLEA FOR PROPHYLAXIS AGAINST THE CHANCER, IN CASES OF TRAUMA, HERPES PREPUTIALIS, VERRUCA, ETC.—M. Zigler, New York City. *American Medicine*, 1918, vol. xiii, p. 490.

The tendency of the times is preventive medicine; and accordingly the author desires to make a plea for the diminution of the frequency of chancre of the penis. He feels that this can be accomplished by starting a propaganda among physicians to remove any or all conditions about or on the penis which are likely to prove points of entry for specific infection. Be these abnormalities warts, inflammations, herpes, cuts, abrasions, or operative incisions, all should be cleared up before the patient is allowed to have intercourse. In this way the likelihood of spirochete pallida infection is greatly diminished by getting rid of the seat of lowered resistance. Whenever there is frequent tearing of the prepuce or frenum during intercourse, advise the application of 30 per cent calomel ointment, the same to be thoroughly rubbed in for twenty minutes. Insist upon sexual abstinence until the tear is thoroughly healed. If possible a subsequent circumcision is to be performed. Warts and herpes are not only apt to cause abrasions, tears, etc., during the act of intercourse, because of their mechanical presence, but they also

predispose to the collection of smegma and secondary infection. They thus denude the skin and mucous membrane of the penis and prepuce, and thereby cause small ulcers which open the field of spirochete pallida invasion. It may seem to be a very minor point to us medical men, and it certainly is not a new one, that abrasions, warts, balanitis, herpes, etc., are very apt to be the sites of infection of spirochete pallida. Warts and also balanitis are to be treated medically or surgically—depending on what conditions are present. A prepuce which tears readily during intercourse should be circumcised.

**THE STIGMATA OF ABRAMS IN HEREDITARY SYPHILIS.**—Albert Abrams, San Francisco, Cal. Medical Record, 1918, vol. xciv, p. 103.

If the subject faces the geographical west feet on a grounded plate and the hands are elevated in proximity to a window, it will be noted after thirty seconds that a circumscribed pallor is demonstrable at the terminal phalanges of all the fingers, notably the little fingers, at definite points, at the palmar surface of the terminal phalanx and on the inner surface and extreme end in heredosyphilis. In acquired syphilis, the circumscribed pallor on the palmar surface is not demonstrable but is seen in the other area only (extreme end). It is evident that mere elevation of the hands is productive of some anemia but the latter is universal and not circumscribed. The hands should be manipulated in relation to the light so as to bring the anemic areas into evidence if not readily seen.

**THE RELATIVE EFFICIENCY OF THE DIFFERENT MERCURIAL PREPARATIONS IN THE TREATMENT OF CONGENITAL SYPHILIS IN INFANTS AND CHILDREN AS DETERMINED BY QUANTITATIVE ANALYSIS OF THE MERCURY ELIMINATED IN THE URINE.**—Walter Reeve Ramsey, St. Paul, Minn. Archives of Pediatrics, 1918, vol. xxxv, p. 338.

In infants, and children, mercury when given by the mouth, by inunction, or subcutaneously, is excreted at least partly by the urine. In newborn infants and older children, mercurial ointment when placed in contact with the skin, without any friction being used (protected and sealed by wax paper from being volatilized and inhaled) is taken up by the skin and eliminated in the urine and continues to be excreted in the urine for some time after all treatment has been discontinued. By inunction (with rubbing) mercury is readily taken up by the skin and eliminated in the urine and continues to be eliminated for a considerable time. When inunction is given, the maximum daily amount of mercury is usually eliminated during the following 24 hours, smaller amounts being eliminated for a variable time. Where continuous inunctions are given there is an accumulation in the system and considerable amounts are eliminated at intervals with only traces in between. It is therefore probable that it is unnecessary to have

mercury in contact with the skin, either with or without rubbing, as often or as long as has been generally thought necessary. This, however, must be determined by further clinical investigation. Mercury salicylate, suspended in oil and given subcutaneously, continues to be eliminated in the urine in appreciable amounts for as long as 8 days, the daily amounts eliminated varying widely. It is therefore probable that repetition of the treatment, not oftener than at intervals of 8 days, would be sufficient. Mercuric chloride by the subcutaneous method, a favorite method in congenital syphilis, continues to be eliminated for 8 days. In all cases where mercuric chloride was used, either by mouth or by the subcutaneous method, protein was found in the urine. Calomel  $\frac{1}{4}$  grain, every 2 hours, for 4 doses and gray powder  $\frac{1}{2}$  grain continued to be eliminated in appreciable amounts in the urine for as long as 9 days, the maximum amount being eliminated during the 24 hours following administration. It is therefore probable that the daily use of any of the mercurial salts in the amounts usually prescribed, is unnecessary and presumably harmful.

THE TREATMENT OF SYPHILIS WITH NOVARSNOBENZOL (BILLON).—Erwin P. Zeisler, Chicago, Ill. *Urologic and Cutaneous Review*, 1918, vol. xxii, p. 502.

Novarsenobenzol is a safe and effective remedial agent in the treatment of syphilis in all its stages. It is clinically and serologically equally as effective as neosalvarsan. Concentrated solutions are to be preferred on account of the freedom from reaction and simplicity of the technic.

REACTION FOLLOWING ADMINISTRATION OF NEOARSPHENAMINE (NEODIARSENOL BRAND).—K. M. Richardson, Rankin, Ill. *Journal of the American Medical Association*, 1918, vol. lxxi, p. 279.

A strong married woman, aged 36, weighing 175 pounds, presented herself for treatment for the secondary stage of syphilis with a 100 per cent Wassermann reaction. During the fifteen months preceding she had received six intravenous injections of the German-made neosalvarsan without any reaction. One ampule of 0.3 gm. of the neodiarsenol brand of arsephenamine was dissolved in 10 c.c. of distilled water previously boiled and then cooled to body temperature. The solution was cloudier than the imported product. Thirty seconds after the entire dose was given the patient began to gasp for breath and complained of tingling in her fingers and hands. She became almost pulseless, her pupils dilated, and her eyes rolled back as if she were dead. The stimulant closest at hand was aromatic spirits of ammonia, which was placed to her nose. She began to rally after a moment, and then became nauseated but could not vomit. Her head



began aching very severely. The author gave her a hypodermic strychnin sulphate, 1/30 grain, for her pulse was still very weak and rapid. This dose was repeated fifteen minutes later. After one and one-half hours she was able to ride home in a car. All symptoms had abated except weakness and the headache, which remained about five or six hours, after which she was perfectly normal.

**INTRARECTAL ADMINISTRATION OF ARSPHENAMINE.**—Augusto S. Boyd and Morris Joseph, Panama, R. P. *Journal of the American Medical Association*, 1918, vol. lxxi, p. 523.

The intrarectal administration of arsphenamine is a successful method of treating syphilis and relapsing fever. The untoward effects are practically eliminated by slower absorption. The method requires no special skill in administration, and can be entrusted to a nurse or to the patient himself. The dosage can be increased by this route and given as often as every three days. It is the method of choice in nervous subjects, in obese or very anemic women, and in children and it offers at least the same curative value as the intravenous route.

**CERTAIN REACTIONS FOLLOWING THE INTRAVENOUS INJECTION OF SALVARSAN AND NEOSALVARSAN, THEIR SYMPTOMS AND TREATMENT.**—Barker Beeson. *Medical Review of Reviews*. December, 1916.

The following suggestions are of value in helping to prevent untoward symptoms after an injection: (1) The use of plain, freshly distilled water as the vehicle. It should be prepared the same day it is to be used. (2) Employ a distillation apparatus which is entirely glass, preferably Jena. (3) The solution of salvarsan should be rendered alkaline, and then a slight excess, one or two drops of 15 per cent sodium hydroxide is added. (4) The initial dose of salvarsan should not exceed 0.30 grams, of neosalvarsan 0.45 grams. As a rule one should not exceed 0.6 grams of "606," or 0.9 when giving neosalvarsan. (5) Seven to ten days should constitute the usual interval between doses. In exceptional cases they can be given four to five days apart. (6) The urine should be examined in all cases previous to the injection. (7) Be cautious in giving these drugs to alcoholics and nephritics also to those who have cardiac lesions or acute inflammation of the upper air passages. (8) Always give the injections on an empty stomach. Don't allow any solid food until the next day. (9) Have the patient go home at once after the injection and remain quiet for the rest of the day.

**COMBINATION OF ADRENALINE WITH ARSENOBENZOL.**—Perin. *Journal de medecin et de chirurgie pratiques*, 1918, vol. lxxxix, p. 218.

The author has written a thesis with the above title, an abstract of which appears in the above periodical. Since salvarsan may give rise

to an intense vasodilatation, especially when used in its acid form, and incidentally determine severe accidents such as serious apoplexy, it occurred to the writer to combine with it adrenaline. The drugs are not to be injected together but at the very instant of the nitritoid crisis, so called because the sudden vasodilatation suggests that due to amyl nitrate, a milligram of adrenaline is thrown under the skin or into a muscle, the dose being repeated if necessary until 4 milligrams shall have been given within the first hour or two. The ill effects of the arsenical drug are regarded as due purely to the mechanical factor, the sudden congestion and serious effusion which is always serious and at times fatal. There is no mention of any actual trial of this remedy.

THE TREATMENT OF SYPHILIS.—T. P. C. Kirkpatrick, Dublin. The Dublin Journal of Medical Science, 1918, vol. cxlv, p. 273.

The earlier after infection that efficient treatment of a patient is undertaken the better the prospect of a quick and complete cure. This has been demonstrated again and again by reliable figures recorded by different writers. On this is based the so-called prophylaxis against syphilis, which is merely early treatment before the spirochete has had time to establish itself at the site of inoculation. The adoption of such a method has given rise to much controversy, but it is outside the purview of our present discussion. Efficient early treatment must always include local treatment of the site of inoculation, whether by inunction, excision, or the cautery, as well as general treatment of the patient. Local treatment by itself, however efficient, will not always prevent the supervention of general symptoms, once the site of inoculation has been made manifest by the local reaction, or the development of the chancre. Such local treatment, however, is of great value as an aid to general treatment. Patients who have passed beyond the primary stage of the disease require a much more prolonged course of treatment than those who are efficiently treated in the primary stage of the disease. No person can be pronounced cured of the disease so long as there is any evidence of living spirochetes in the body, no matter how prolonged or vigorously treatment has been carried out. Persons who have been infected with syphilis and who are not cured, even though they may cease to be infectious in the ordinary sense, are always liable to a recurrence of symptoms, the so-called late tertiary manifestations of the disease. Syphilis of the central nervous system may be present as an active disease even though the patient's blood serum has for long periods given a negative Wassermann reaction. In such patients the Wassermann reaction of the cerebrospinal fluid will generally be found to be positive. The only reliable methods of proving the existence of actual syphilis is the demonstration of the presence of the spirochete in the patient or the demonstration of a positive Wassermann reac-

tion in the blood or body fluids. Efficient treatment of syphilis includes the administration of salvarsan or some of its substitutes.

**THE TREATMENT OF SYPHILIS.**—George E. Pugin Meldon, Dublin. The Dublin Journal of Medical Science, 1918, vol. cxlv, p. 286.

The treatment should continue for three months, and should consist of intravenous injections of salvarsan and the administration of mercury. Three weekly injections of salvarsan, and then three at fortnightly intervals, combined with mercury during the whole period, and continued for several weeks afterwards. The Wassermann reaction should be taken before commencing treatment, if the treatment be not delayed by so doing. The serum should also be tested frequently during treatment in order to see how soon it becomes negative, and should be watched afterwards for a couple of years. If such treatment be started before the patient has developed a positive Wassermann, and the Wassermann has remained negative, or (which is more frequently the case) has become positive for a short time and then returned to a negative reaction, then the author believes that this course of treatment is sufficient to cure. If, on the other hand, the Wassermann reaction is already positive before treatment, the patient may require a second similar or modified course.

**CURABILITY OF SYPHILIS.**—De Freitas. Brazil-Medico, 1918, vol. xxxii, p. 41.

The author classes *sterilisatio magna* with the elixir of life and philosopher's stone as a something unrealizable in practice, illustrating his contention with a series of cases. One subject with old syphilis and strongly positive seroreaction suffered with a distressing headache which resisted alike all sedatives, intensive mercurial treatment and injections of old and new salvarsan, only to recover with ridiculous promptness after the ingestion of two grams of potassium iodide. A second patient with history of syphilis, strongly positive seroreaction, fever and osteocopic pains, developed a hematemesis which resisted all styptic medication to yield promptly to injections of mercury. In a third subject with stenosis of the esophagus and positive seroreaction hectine injections were curative. On the other hand, salvarsan may also effect striking clinical cures, as in a case of a large ulcer on the lower third of the leg with positive seroreaction, which healed after a single intramuscular injection.

**RESULTS IN TREATMENT OF PARESIS BY INUNCTIONS OF MERCURY AND DRAINAGE OF THE CEREBROSPINAL FLUID.**—Alan D. Finlayson, Warren, Pa. The American Journal of Insanity, 1918, vol. lxxiv, p. 622.

Fourteen paretics, who had been showing symptoms from nine months to several years, received daily inunctions of mercurial oint-

ment 50 per cent. Every tenth day a lumbar puncture was made and from 20 c.c. to 40 c.c. of fluid withdrawn, the amount depending on the pressure and the rapidity of the flow. A Wassermann reaction was done, using the blood serum; a globulin test, cell count, Lange's colloidal gold test, Wassermann reaction and a chemical test to determine the presence of mercury were done, using the fluid. In seven, or 50 per cent of the cases the blood Wassermann became negative and remained so for varying periods of time; one case had a negative blood at the time of admission and it remained so throughout the period of observation. In 6, or 43 per cent of the cases, the spinal fluid became negative and remained so for varying periods of time. In no instance did the blood or spinal fluid become negative and remain so. All cases had negative globulin tests at one or more examinations, but, with the exception of one case, more positives than negatives were obtained. The cell count showed an irregular decrease in all instances. In 4, or 28 per cent of the cases, the colloidal gold became negative, that is, was neither paretic nor luetic in type, but all showed "paretic curves" at some later examination. After 15 months' treatment a trace of mercury was found in 500 c.c. of grouped spinal fluids. No mercury was found on previous examinations. One case showed a good remission mentally, but all the serologic findings remained strongly positive. Another case did not improve quite so much, but approached a state termed a remission, and has shown some negative serologic findings. The remaining 12 cases showed no greater mental or physical changes than would be found in a similar group of untreated cases. The lack of correlation between the serological findings and mental conditions leaves little ground on which to base definite conclusions as to the value of treatment.

DIAGNOSIS AND TREATMENT OF SYPHILIS OF THE CENTRAL NERVOUS SYSTEM WITH SPECIAL REFERENCE TO THE USE OF NOVARSENO-BILLON.—Hildred Carlill, London, England. *The Lancet*, 1918, vol. exciv, p. 249.

The possibility of a syphilitic basis should be considered in every case of nervous disease. Nervous syphilis can be proved by examination of the cerebrospinal fluid. The examination of the serum, whether the Wassermann reaction is positive or negative, is of little value in the diagnosis of these cases. Provided that the diagnosis is made early, and prompt treatment given in adequate quantity, syphilis of the nervous system appears to be curable in very many cases. The real result of treatment can only be determined by repeated examination of the cerebrospinal fluid, hence the absolute necessity of painless lumbar puncture. Cases in which this operation has been contraindicated have not been observed. Some cases of curable meningo-vascular syphilis are diagnosed as incurable dementia paralytica, and

treatment is withheld. Often the precise diagnosis can only be made by watching the result of treatment; therefore all cases should have treatment. Even in some cases of long-standing *tabes dorsalis* the syphilis appears to be entirely curable by treatment, and in nearly all cases symptoms can be greatly alleviated by "606." Novarsenobillon, in the author's hands, has proved a safe and most efficient remedy against the protean ravages of the *Spirochete pallida*. Galyl is not recommended. The outlook of sufferers from early neurologic syphilis is very bright, and will be brighter still when the general standard of knowledge of neurologic diagnosis is less inadequate than it is today. If the profession and the public seize and apply our present knowledge of syphilis it is not too much to hope that the future generations of students will learn of *tabes dorsalis* and *dementia paralytica* only from the textbooks. Abolition of ankle jerks is an early sign, and often the only one, of arsenical neuritis, and may be demonstrated in the absence of any subjective symptoms.

A DISCUSSION OF SOME EARLY PHASES OF SYPHILIS OF THE NERVOUS SYSTEM.—C. F. New, Indianapolis, Indiana. *Mississippi Valley Medical Journal*, 1918, vol. xxv, p. 114.

For all practical purposes every case of syphilitic infection becomes potentially a probable case of cerebrospinal syphilis. With our present methods of treatment the cure of syphilis of the nervous system is doubtful. There may be and probably is a cure for the majority of cases, but to obtain it there must be a change from the methods of treatment heretofore followed. Every case of syphilitic infection before discharged from the treatment and observation should have an examination of the spinal fluid made, as well as of the blood, and if found positive be given treatment accordingly.

SOME QUALITATIVE AND QUANTITATIVE TESTS FOR ARSPHENAMINE (3, 3'-DIAMINO-4, 4'-DIOXY - ARSENOBENZENE DIHYDROCHLORIDE) AND NEO-ARSPHENAMINE (SODIUM-3, 3'-DIAMINO-4, 4'-DIHYDROXY - ARSENOBENZENE - METHANAL - SULPHOXALATE). — C. N. Meyers, United States Public Health Service. *Public Health Reports*, 1918, vol. xxxiii, p. 1016.

The data indicate that the rate at which digestion is allowed to proceed is a factor which influences the final result to a very considerable extent. But they also show that the results are low even when digestion is carried out very slowly. It appears, therefore, that this method in its present form is objectionable. It is possible that greater accuracy might be attained by condensing the fumes which escape during digestion, reuniting the distillate with the contents of the Kjeldahl flask previous to neutralization, and finally titrating the mixture. Work along this line is, however, necessary before a

positive statement may be made. The method of Lehmann, with the slight modifications recommended in the footnotes, is accurate and reliable. It is simple, requires but small quantities of inexpensive reagents, and can be completed in about one and one-half hours. It, therefore, appears to be superior to any of the other methods mentioned for the routine analysis of these products.

THE PRESENT POSITION OF TREATMENT OF SYPHILIS.—H. S. Matson, *Peona Indian Medical Gazette*, 1918, vol. liii, p. 130.

The present position of the treatment of syphilis is that in the intramuscular injection of Arsphenamine (Salvarsan) one finds the most satisfactory solution of the problem. Trivalent arsenic can in this way be introduced into the organism in such doses as to be able to exert its selective effect without damaging the host. So far no other chemical compound used in the treatment of syphilis has been comparable to arsеноaminophenol and its salts in therapeutic efficiency. The relation of the radicles of arsеноaminophenol in the phenol ring forms a combination which is destructive to and selective for the spirochete of syphilis in the same way and probably to a greater extent than the quinine grouping to malaria infections. The amine groups are of paramount importance to conferring protection against the toxic effects of arsenic. Interference with them (i. e., the formation of substitution products with their hydrogen atoms) may increase the solubility or stability of the compound, but tends to diminish the therapeutic value. The diminution seems to bear a direct relation to the extent of such interference. The introduction of such metals as aluminium in the place of arsenic has so far found only a limited application, the metal to ensure the effectiveness of the new compound must be in close association with an amino-phenol ring, i. e., directly combined with a carbon atom of the ring, not merely as the salt of an amino-aryl acid.

THE PREVENTION OF CONGENITAL SYPHILIS BY ANTILUETIC PRENATAL THERAPY.—H. Lissner, University of California Medical School, San Francisco, Cal. *California State Journal of Medicine*, 1918, vol. xvi, p. 387.

There are many cases of congenital syphilis in the world. Most cases of congenital syphilis have been preceded by two or three miscarriages, premature births or stillborn children due to syphilis. The vital problem of repopulating the world after this war involves the serious consideration of this appalling wastage of life. Proper treatment of acquired syphilis before pregnancy will to a considerable extent diminish this waste, which can at best be only partially controlled. But intensive treatment of every syphilitic mother during

her pregnancy will prevent miscarriages, premature births, and stillbirths due to syphilis, in the vast majority of cases and produce a live child at full term who will not develop congenital syphilis, in the majority of cases. Such treatment does not interfere with the normal course of pregnancy, labor or puerperium. Such antenatal therapy should be widely advocated by medical men of prominence and influence, in order that it may become a well-established routine procedure. Immediate widespread adoption of this method will insure a large increase in the future population of the world.

**PERMANGANATE OF POTASH IN THE TREATMENT OF SYPHILIS, PHAGEDENIC ULCERATIONS AND SOFT SORES.**—M. Kamel Barradah, Cairo, Egypt. Privately Printed Brochure, Cairo, 1918, p. 14.

The drug is dissolved in distilled water in the proportion of 0.05 of the drug in one c.c. of distilled water, and storing in sterilized ampules or bottles. The solution keeps well. The apparatus used is the ordinary one for salvarsan. The operation is practically the same only the following points need be observed: Previous preparation of patient is unnecessary. A thick needle with a large lumen must be used. The biggest vein has to be chosen. This allows the fluid to pass in as quickly as possible so as to lessen the period of pain. The dose (5 c. c. of the solution) is to be diluted with 50 c. c. of distilled water in the cylinder. During the injection patients suffer pain at the site of the needle, then along the arm, upwards to the axilla and chest; with flushing of face, whirling in the head and a temporary slight deafness which continue with variable severity for half a minute after the injection. This was never followed by ill effects. The after-treatment is practically nil. Patients have undergone the severest exertion without the least risk. The author has had a patient taking his motor cycle ride immediately after injection; and another one had a sulphur bath of 3 hours duration to cure his scabies immediately he quitted the table. No trouble or complications occurred. Some cases have suffered from a slight swelling of the arm at the site of injection, which apparently may be due either to a slight sepsis or possibly to a local thrombosis which gradually recovered under hot application. No fatal cases or even dangerous cases occurred. Permanganate of potash has proved to be a specific value for soft sores and phagedenic ulceration although its action can not be at present explained. It is of less value for chancres and syphilitic rashes. It is of no value for condylomatous lesions, mucous patches, general adenitis, or gummatous ulcerations. It appears to be of no use in malaria, although only one case tried. It is the best drug to be given when for some reason or other mercury, salvarsan, or its substitutes are contraindicated. Permanganate has no contraindication whatever, and although somewhat painful during its administration, its value for the disease, and the

fact that patients need not be prepared or wait in hospitals for a possible reaction, greatly adds to its benefit. Further trials are now made to alleviate the pain. Trials with permanganate alternately with intramine are being commenced and the results will be published in due course.

TREATMENT OF SYPHILIS, REPORT OF SPECIAL CLINIC FOR SYPHILIS, TORONTO GENERAL HOSPITAL.—W. T. Williams, Toronto, Canadian Medical Association Journal, 1918, vol. viii, p. 630.

Considering the class of cases that have been dealt with at this clinic, the results of treatment are not at all discouraging. Of the five hundred cases so far treated, only about 29 per cent have been early, while 71 per cent have been in the later stages of the disease. They have managed to secure negative Wassermanns on only seventy of these cases on an average of seven and a half doses of 0.5 gram diarsenol plus four and a half intramuscular injections of mercury. Of the 70 cases, 23 were early and 47 in the later stages. Practically all of the late cases were given in addition mixed treatment of mercury and potassium iodide. Twenty-four cases had a return to positive Wassermann, thirty-five still remain negative, while eleven of them passed from our control. About 80 per cent of all cases experienced relief or freedom from all symptoms, which at any rate is encouraging. Reactions from diarsenol are fairly frequent and occur at times while the dose is being administered. One of the most frequent is a feeling of fullness in the stomach, a full, bursting sensation in the head while the patient becomes intensely flushed with dilated pupils and has an apparent difficulty in breathing. This, however, soon passes off and the patient is none the worse for the experience. Occasionally there is quite severe nausea which remains for a day or two.

THE TREATMENT OF SYPHILIS AT CAMP TRAVIS.—William H. Guy, Pittsburgh, Pa. Journal of Cutaneous Diseases, 1918, vol. xxxvi, p. 444.

A standard technic has been adopted and is used by all regimental surgeons, injections being given in the evening so that the men do not lose any time. The author begins with  $\frac{1}{2}$  to  $\frac{3}{4}$  grain and increase at the rate of  $\frac{1}{4}$  grain weekly if well tolerated until 2 or  $2\frac{1}{2}$  grains are given at each dose. As has been noted by others, he finds that the amount of mercury that a patient will tolerate bears no relation to his body weight. In cases in which the diagnosis is made by the dark-field method, treatment is more intensive than in the later stages of the disease, because we may then reasonably expect a prompt cure, provided the individual is physically able to stand intensive treatment. It is by no means a settled question as to how intensive this treatment should be, but every one agrees that it should be as intensive as possible with safety. There are those who believe that every syphilitic



should receive an arsphenamine (salvarsan) injection on each of three or four successive days, followed by a course of mercury to toleration as routine treatment in patients physically fit. A few selected cases with primary lesions have been treated in this manner at Camp Travis with good results. Though too early to draw conclusions, a positive Wassermann reaction has never been obtained in any of these cases. The routine treatment in primary cases comprises 0.1 gm. of arsphenamine (salvarsan) for each 30 pounds of body weight, repeated twice the first week, followed by the usual weekly arsphenamine (salvarsan) and mercury for ten weeks; then the therapeutic rest for five weeks, after which a Wassermann test is made and the course repeated; then the case is kept under observation, Wassermann tests being made at intervals. In tertiary and certain late secondary cases routine courses are given plus the iodide of potassium to saturation. To date about 400 cases of syphilis have been handled, some of them only for a short time because of transfer from place to place, others having just recently come under observation, and the number of cases under treatment is of course increasing. At present about 350 injections of the arsenobenzol brand of arsphenamine and the same number of treatments with mercury are given weekly.

**FURTHER OBSERVATIONS ON THE TREATMENT OF YAWS WITH CASTELLANI'S MIXTURE.**—L. E. Guerrero, E. Domingo, and M. Arguelles, Philippines. *Philippine Journal of Science*, 1918, vol. xiii, p. 196.

The author's results confirm the conclusion of Castellani that the diverse manifestations of frambesia heal under the influence of his treatment. The cure of recent infections is nearly as marvelous as that by salvarsan and neosalvarsan. They can not assert as yet whether or not the cure is permanent, since only a limited number of cases remained under their observation for a long time. They believe however, that the continuation of the treatment after the lesions have healed (from five to ten days' treatment with intermissions of from ten to fifteen days) will insure a permanent cure.

**INTRASPINAL INJECTIONS OF NOVARSENOBENZOL IN NERVOUS SYPHILIS.**—Levy-Bing, Gerbay and Dagnam-Bouveret. *Annales des Maladies Veneriennes*, 1918, vol. xiii, p. 401.

Syphilis of the nerve centers is largely an independent process, which can only be reached by direct injection of remedies. Mercury has now been exhibited in this manner for many years with varying results. Much more constant are certain untoward effects of this treatment; and as a result, syphilographers have had to look elsewhere for a remedy. Neosalvarsan, if used in a certain dosage, does not provoke a reaction, 5 mg. being the maximum safe dose. Gaines practiced 100 injections into the spines of 70 subjects and claims good results. The authors cite a case in which they employed this

method after other forms of intensive treatment had failed to clear up the cord symptoms. After one injection the Wassermann of the spinal fluid was still positive and the dose was doubled. Puncture showed a notable reaction in the fluid and the dose was doubled for a second time and followed by severe reactionary phenomena, paraplegia setting in and augmenting until it became total. To resume, a man with syphilitic meningitis treated by frictions and intravenous injections of salvarsan with relief of symptoms but without disappearance of evidences of infection of the spinal fluid was treated with large doses of novarsenobenzol given by intraspinal injection with the production of total paraplegia which has after 2 months shown no tendency to improve.

**INTRASPINAL TREATMENT OF CEREBROSPINAL SYPHILIS.**—Clyde L. Cummer and Richard Dexter, Cleveland, Ohio. *Journal of the American Medical Association*, 1918, vol. lxxi, p. 792.

Five years' experience with the use of arsphenaminized serum shows that: Properly employed, it is not in any sense dangerous. Excellent evidence of its efficacy is offered by the patients who repeatedly endure the painful though harmless reactions which frequently follow intraspinal injections. Little or nothing can be expected in fully developed paresis. Much advantage is derived in many cases of tabes dorsalis and syphilitic meningitis when the other methods have proved inefficient. The results of the laboratory examinations of the blood and particularly of the spinal fluid must be considered as an integral part of the clinical picture, both in the diagnosis and in the direction of the treatment. The improvement in the satisfactory cases has been so definitely consequent on active treatment, and the ground gained over a period of years has been held so well in spite of the lack of recent treatment, that it can not be explained as a coincident remission in the progress of the disease.

**THE TREATMENT OF LOCOMOTOR ATAXIA AND GENERAL PARESIS BY INTRASPINOUS INJECTIONS OF BICHLORID OF MERCURY.**—R. B. McBride, Dallas, Texas. *Journal of the Southern Medical Association*, 1918, vol. xi, p. 410.

Feeling as he does that his work has clearly demonstrated to him that bichloride of mercury intraspinaly, and alone, will render the spinal fluid negative to all tests and relieve symptoms for a time, but as the blood remains a constant source of contamination, and as intravenous medication is known to clear the blood stream and to act beneficially to some extent in these conditions under consideration, it is now the author's practice to administer both intravenous and intraspinal medication. At present it is his habit to give, on an average, four to six of the former to one of the latter, giving a total of from four to six bichloride spinal injections. Symptoms of the case

along with the serum and the spinal fluid examination are our guide as to when this routine should be repeated, and it will be necessary to repeat such routine one or more times.

Results obtained by this combined method are very gratifying and the treatment leads to an absolute cure so far as clinical symptoms are concerned, for at least a good period of time. They have not yet had sufficient time to feel certain, however, that any of these cases are permanently cured. So far none diligently treated has fallen down, but if the relief were only temporary it would be sufficient to compensate for any burden that such treatment as outlined entails, and he would hope by successive series of treatments just as is done in constitutional syphilis, to accomplish the desired result. Life is made worth the living and patients who are dependents are rendered capable of earning livelihood.

**SOME FURTHER CONSIDERATIONS CONCERNING THE TREATMENT OF NEUROSYPHILIS.**—C. Eugene Riggs, St. Paul, Minnesota. *Journal of the American Medical Association*, 1918, vol. lxxi, p. 161.

All of the three methods (the intraspinal, intracranial and the intensive), in the light of our present experience, may, therefore, be called efficient. This is particularly true as regards cerebrospinal syphilis and tabes dorsalis, and even in paresis, the most hopeless of all the manifestations of syphilis. The accomplishment of these two purposes has in a measure met success—certainly not with a lamentable failure. It is a well-known fact that the percentage of remissions is much greater in treated than in untreated paresis.

**THE EARLY DIAGNOSIS AND TREATMENT OF TABES DORSALIS.**—Lloyd Thompson, Hot Springs, Ark. *Journal of the Arkansas Medical Society*, 1918, vol. xiv, p. 239.

Sensory symptoms are both subjective and objective, the former being in the majority of cases the earliest symptoms of the disease. The subjective sensory symptoms consist of pains of varying location and intensity, the most characteristic ones being the so-called lightning or lancinating pains, and certain paresthesias. Other pains of a less severe nature but more permanent are noted. The chief of these is the so-called girdle pain which the patient describes as the sensation of a tight belt around the body. Certain paresthesias such as numbness, formication, tingling, prickling, the sensation of walking on velvet, as if cold water were running over the body, the feeling of cobwebs on the skin, etc., are often observed.

Of the objective sensory symptoms the most frequent is analgesia which affects the cutaneous surface, and also the bones, joints and muscles. Areas of hyperalgesia are also common but less symmetrically located and less frequent. Anesthetic areas are very frequently observed in tabes. A striking symptom in some cases is an impairment

of stereognosis, the patient being unable to distinguish by the sense of touch such objects as a key or coin. Motor symptoms in tabes consist of ataxia, which may be more than that of locomotion, involuntary movements, and paralyses. The ataxia is not as a rule, an early symptom of tabes, usually developing after sensory symptoms have been present for some time. The ataxia, however, may be the first symptom to call the attention of the patient or the physician to the true nature of the condition. The paralyses found in tabes consist of monoplegia, hemiplegia and paraplegia, paralysis of the tongue and larynx, facial paralysis and ptosis. Anomalies of pupillary reaction are found in the vast majority of tabetics. Of these the so-called Argyll Robertson pupil is the most important. This phenomenon, which consists of a loss of light reflex, while the reaction to accommodation remains intact, is found in from 50 to 70 per cent of cases. Reflex Symptoms. Diminished or absent deep reflexes, especially the knee jerk, is one of the earliest and most frequent symptoms of tabes. It is usually bilateral but may be confined to one side. The superficial reflexes may or may not be disturbed. The most important and frequent of the visceral symptoms are those referable to the stomach. The so-called gastric crises, which are of sudden onset, may occur very early in the course of tabes, in fact, may be the only symptom observed, the patient being treated for other types of gastric disorder. Intestinal crises are of rather rare occurrence, are characterized by marked diarrhea but without pain. The bladder is the seat of some of the earliest and most constant symptoms of tabes. Nephritis crises have been described, but may be due to renal colic. The genital organs are very frequently affected in tabes. Diminution of the sexual appetite and even impotence are observed in about 50 per cent of the cases and is sometimes preceded by an excessive sexual appetite. Laryngeal crises occur quite frequently and consist of spasms of the laryngeal muscles. The bones are very frequently the seat of spontaneous fracture due to rarefaction and decalcification.

The so-called Charcot's joint, which sometimes occurs in tabes, usually is first manifested by an abnormal range of motion. The author's experience now covers more than 250 injections, and the clinical results are very satisfactory.

## BOOK NOTICES

(Books for review should be sent to Dr. W. H. Deaderick, Associate Editor, Dugan-Stuart Bldg., Hot Springs, Arkansas.)

**SYPHILIS WITH SPECIAL REFERENCE TO ITS PREVALENCE AND INTENSITY IN THE PAST AND AT THE PRESENT DAY, ITS RELATION TO PUBLIC HEALTH AND THE TREATMENT OF THE DISEASE.**—A discussion opened by Sir Henry Morris, F.R.C.S., Norman Moore, M.D., D'Arcy Power, F.R.C.S., and F. W. Mott, M.D., F.R.S. Quarto, 214 pages. Price \$1.50. Longmans, Green and Company, London, New York, Calcutta and Bombay, 1912.

This work consists of addresses by Moore, Power and Mott before the Royal Society of Medicine and a discussion by its members, being summarized by Sir Henry Morris. The history of syphilis is fully treated, particularly the question of its importation from the western hemisphere in 1493. The consensus of opinion elicited through the addresses and discussion is that the treatment with mercury without arsphenamine will not be entirely supplanted. The address of Mott on the relation of the disease to public health including congenital syphilis is especially valuable. The free discussion of the proceedings makes the work particularly interesting.

**SYPHILIS FROM THE MODERN STANDPOINT.**—By James McIntosh, M.D., Grocers' Research Scholar, and Paul Fildes, M.B., B.C., Assistant Bacteriologist to the London Hospital. 222 pages. Illustrated. Cloth, \$3.25. London, Edward Arnold. New York, Longmans, Green and Company, 1911.

The object of this work is to collect into one systematic whole the various remarkable advances made in the domain of syphilis within the eight years preceding publication. The subjects taken up systematically are: the history of syphilis, spirochetes, the demonstration of the spirocheta pallida and its pathogenicity, the histopathology of syphilitic tissues, immunity, the Wassermann reaction, the effect of specific treatment upon the reaction, its clinical value and the treatment of syphilis by salvarsan. The authors explain that the small space given to mercury in the treatment of syphilis is due to their lack of any clear information regarding it. The subjects within the scope of the work are treated extensively and impartially. References at the end of each chapter add to the research value of the volume. The monograph is a very valuable addition to the literature on syphilis.

**DISEASES OF THE MALE URETHRA.**—By Irvin S. Koll, M.D., Professor of Genitourinary Diseases, Post-Graduate Medical School and Hospital, Chicago. Octavo of 151 pages, with 123 illustrations, several in colors. Cloth, \$3.00 net. Philadelphia and London, W. B. Saunders Company, 1918.

About half of the work is devoted to gonorrhea, by far the most important disease of the male urethra. The author states that sixty per cent of patients with gonorrheal urethritis, if seen within the first twenty-four hours after the discharge has begun, can be cured in from five to ten days. The treatment consists of rest in bed for the first two or three days, the drinking of large quantities of water and urethral instillations of albargin, the specific details of which are minutely given. The characteristic of the book throughout is that the author gives his own treatment in great detail making the work essentially practical. The paper is of highest grade to take care of the 123 illustrations, which are excellent and add to the clearness of the description.

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